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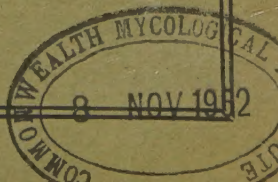
[No. 9

## MAIN CONTENTS

PAGES	PAGES
The Analysis of Equilibrium in Malaria ... 813-829	Leprosy ... 870-875
Summary of Recent Abstracts. VII. Helminthiasis ( <i>con- cluded</i> ) ... 830-837	Helminthiasis ... 875-891
Malaria ... 837-846	Deficiency Diseases ... 891-892
Blackwater Fever ... 847	Haematology ... 892-894
Trypanosomiasis ... 847-849	Venoms and Antivenenes ... 894-895
Leishmaniasis ... 849-852	Dermatology and Fungus Diseases ... 895
Fevers of the Typhus Group ... 853-854	Tropical Ophthalmology ... 896-901
Bartonellosis ... 854	Tropical Ulcer ... 902-904
Yellow Fever ... 855-856	Miscellaneous Diseases ... 904
Rabies ... 856-857	Protozoology : General ... 904-908
Plague ... 857-858	Entomology and Insecticides : General ... 908-910
Amoebiasis and Intestinal Protozoal Infections ... 858-868	Laboratory Procedures ... 910-911
Relapsing Fever and Other Spirochaetoses ... 868-870	Reports, Surveys and Miscel- laneous Papers ... 911-916

For detailed Contents see pp. ii, iv, vi, viii, x and xii.

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## BUREAU OF HYGIENE AND TROPICAL DISEASES

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## THE ANALYSIS OF EQUILIBRIUM IN MALARIA

by

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## TABLE OF CONTENTS

	PAGE
Introduction ... ..	813
The Theory of Equilibrium and Stability ... ..	815
Epidemiological Types ... ..	818
Stable Malaria ... ..	818
Unstable Malaria ... ..	819
Epidemic Malaria ... ..	819
Comparison of Theory with Nature ... ..	820
Discussion ... ..	822
Summary ... ..	824
Appendix : Mathematical Argument ... ..	825
References ... ..	828

## Introduction

An effort has been made in previous papers (MACDONALD 1950 *a* and *b* ; 1952) to study the influence of the mosquito malaria-infection rate on the human infection rate, and of the human infection rate on the mosquito infection rate. In the first case the inoculation rate was considered as a constant and the human infection rate as a variable dependent on it ; in the second the process was reversed. Both of these approaches represent some natural happenings, but the normal happening is that they are mutually dependent on each other, and must change in unison until they reach some level of equilibrium at which there is no tendency for further change in either. It is the object of the present paper to study the mechanism of this mutual adjustment, which in ordinary epidemiological terms provides the reason for malaria being endemic or epidemic, for the level at which the disease will tend to stabilize itself and for the ease with which this equilibrium can be upset.



The reasons why insect-borne diseases sometimes occur in endemic and sometimes in epidemic form were first studied by precise means almost simultaneously by ROSS (1908, 1911) and CHRISTOPHERS (1911). ROSS was working on a background of a study of epidemic malaria in Mauritius and set out to analyse probable happenings by mathematical means, trying to see how changes in the factors responsible would influence the amount of disease. He produced a general statement of epidemic happenings, and the theory of the critical level which stated that for any given set of malariological circumstances some minimum number of mosquitoes, above zero, was needed to keep transmission going. If the numbers fell below this level, the amount of disease would progressively decrease to ultimate extinction, and if they were above, it would be maintained or exacerbated. This form of analysis was continued by a number of workers including ROSS (1916), ROSS and HUDSON (1917), WAITE (1910), MCKENDRICK (1912), LOTKA (1923) and KERMACK and MCKENDRICK (1927). The theory of the critical level became well established and it has been estimated in the field by RUSSELL and RAO (1942 *a* and *b*) and VISWANATHAN (1945), and more tentatively by BARBER *et al.* (1936). It has not been measured in Africa, but the work of WALTON (1947) shows that the critical density of *Anopheles gambiae* in Sierra Leone must be extremely low. The generalized theory of epidemic happenings, on the other hand, departed from its original simple form and was deliberately developed as an abstract mathematical study. This was not translated into ordinary terminology or related to field happenings and, in consequence, became neglected.

Christophers based his studies on the epidemic of malaria in the Punjab in 1908 and showed that this part of India suffered from periodic epidemics, the 1908 example being more severe than some others but not otherwise distinct from the series. He showed that the periodic epidemics were associated with certain rainfall characteristics and with an inadequate immunity in the local population, and his correlations were so close that they formed an obvious basis for forecasting future epidemics. The subject was further studied by GILL (1914, 1920, 1921, 1923 and 1928), who developed a method of forecasting Punjab epidemics, based on epidemic potential as shown by past experience, July and August rainfall, the spleen rate, and economic conditions. He also published a unitary theory of epidemics, derived primarily from a study of malaria but applicable to all diseases, in which the important factors were the interplay of transmission and immunity; constant transmission built up a firm immunity which prevented epidemic happenings, whereas interrupted transmission permitted a fall of immunity, followed by an epidemic when transmission was resumed and which built the immunity up past the level at which another epidemic could happen for several years.

Subsequent detailed studies of epidemics have been made in Sind (COVELL and BAILY, 1932, 1936) and in Ceylon (BRIERCLIFFE, 1935; BRIERCLIFFE *et al.*, 1935, GILL, 1935, 1936). The epidemics in Sind were a new phenomenon following the advent of irrigation. The disastrous Ceylon epidemic of 1934 and 1935 was shown, like the 1908 Punjab epidemic, to be only one of a series which could be traced back as far as records would allow. In all of these studies the general interplay of interrupted transmission and varying immunity shown in the Punjab was again demonstrated. It has since been widely taken to explain these periodic epidemic happenings, though Gill's additional postulation of a preliminary epidemic of relapses has not been generally supported.

Extending these local studies to more general conditions, CHRISTOPHERS and SINTON (1926) and CHRISTOPHERS (1949) mapped the epidemiology of



malaria in India, and in the world. They showed that there was a considerable epidemic potential over a large part of India, though fulminant epidemics only occurred in small areas, and also that severe regional epidemics without obvious gross cause were liable to occur in a number of geographical areas. They included the Punjab and Sind, Ceylon, part of north-west Africa, parts of South America and notably Argentina, and perhaps China.

In parallel with this study of epidemic happenings, a number of workers studied more static happenings, on which much light was thrown by the work of SCHÜFFNER (1919), CHRISTOPHERS (1924), WILSON (1936, 1938, 1939) and SWELLENGREBEL (1949). These more static conditions presented a converse picture of stable immunity sufficient to protect against epidemic happenings should transmission be increased. Out of these two complementary lines of study arose a generally accepted theory of happenings, which states that interrupted transmission and low endemicity lead to the production of an unstable immunity, which in turn inclines to the precipitation of periodic epidemics. Steady transmission, not materially changing from year to year, leads on the other hand to the production of a firm immunity which protects the community against outbreaks of the disease.

Personal work in two of the great epidemic areas—the Punjab and Ceylon—has left the writer satisfied that the accepted explanation of periodic epidemics is an entirely satisfactory statement of what happens, but remains completely unsatisfying as a statement of why it happens. The climates of those places are variable, occasional variations are dramatic and have dramatic results, as happened in Ceylon in 1934. These epidemics, however, are recurrent and are not always associated with great climatic changes, but often with minor ones which are difficult to discern without statistical analysis. The chain of cause and effect from rainfall or drought to malaria is clear, but it is not clear why small changes in climate should produce such dramatic changes in the amount of transmission. Equal climatic changes occur in most parts of the world, and in many of them the normal endemic level is as low as or lower than that in the epidemic zones; if the explanation were to be completely satisfying it would have to show why transmission undergoes such dramatically important variations in some places and not in others.

The primary intention of the present work is to study the variability of transmission, and the sensitivity of the endemic level to alterations in it. The process of increase in malaria incidence is a chain of events; there is no reason to think that doubling the number of vectors would merely double the malaria, but there is reason to think that it would lead to a progressive growth, increasing the number of cases which would in turn increase the proportion of infected mosquitoes, and so on. The nature of this growth and the extent to which it would continue before it is in some way brought to an end can only be analysed by a reversion to the method of Ross, with an effort to translate the mathematical symbols back into ordinary epidemiological terms.

### **The Theory of Equilibrium and Stability**

A mathematical statement of the endemic level, and of its sensitivity to changes in the controlling factors, is set out in an Appendix, which is illustrated verbally in the present section. There are two fundamental ideas in the mathematical working; the idea of equilibrium and that of sensitivity. The first refers to the level at which the parasite rate, or other index of the proportion of people affected, will stabilize itself at the end of a period of change. The second refers to the ease with which that equilibrium is upset by changes in the controlling factors.



Equilibrium may be established at zero, that is by extinction of the disease, at some level between zero and 1.0 (0 and 100 per cent.), or at 1.0; expressions (17), (15) and (14) in the Appendix describe the conditions under which each of these ultimate levels may be expected. Those leading to extinction of the disease, or a zero limit, are dependent on the numerical value of all the controlling factors, mosquito density, mosquito longevity, anthropophilism and frequency of feeding, the time of the extrinsic cycle, the infectivity of sporozoites and the human recovery rate. They can be brought together in several ways but best in the form of the maximum (or "critical") density of anophelines which would permit this ending. The resulting expression (17) is essentially the same as that for the "critical level" expounded by Ross, differing only in presentation. Each of the factors concerned in it has a considerable range in nature, so that the conceivable range of critical densities is very great indeed. Limiting consideration to the notorious vectors, numerical assessment suggests a value of roughly 0.02 for *A. gambiae* in its preferred environment and one of about 20 for *A. culicifacies* in its less preferred surroundings, and these roughly correspond with happenings in nature. No great importance is attached to the precise value of these figures, the intention being to illustrate their order, which makes the occurrence of anophelism without malaria very unlikely in the one case and likely in the other, as is in fact the case.

Establishment of equilibrium between zero and 1.0 must mean that an original multiplication of cases was brought to an end in some way, and the mechanism by which this growth is curbed deserves statement, derived from the working but explicable on solely logical grounds. In the case of insect-borne disease, in contrast to direct infections, the mechanism is a dual one. When the original multiplication has proceeded for some time its rate is altered by the rising infection rate in both the man and the mosquito. As these reach material levels an increasing proportion of potentially infective inocula, or feeds, fall on men or mosquitoes which are already infected. Such double infections only produce the epidemiological effect of a single one, and in consequence the rate of multiplication is progressively slowed as the infection rate in man and the mosquito increase, till finally equilibrium is reached.

If one considers this throttling effect as it happens in the mosquito, the extent to which it will occur depends on the height which the infection rate in the mosquitoes reaches. This in turn is greatly dependent on anthropophilism and longevity, the curb being greater in mosquitoes among which these values are high than among those in which it is low. In other words, the curb is less when the disease is carried by many mosquitoes with a low sporozoite rate than when carried by few mosquitoes with a high rate, and, other things being equal, the ultimate level reached will be higher in the first case than in the second.

Expression (15) shows the endemic level and can be used as a general statement if values below zero and over 1.0 are read as being zero and 1.0 respectively. It is influenced by both longevity and man-biting habit in the way described above. As will be shown, however, it is very sensitive to small changes in the value of the individual factors, and no direct numerical comparison with nature is therefore justifiable, because even minute errors in primary assumptions would be grossly magnified in the process. The main value of the expression lies in its use to analyse sensitivity in the manner which follows, though general, but not numerical, conclusions may be drawn from it. An important one is that the mosquito characteristics which lead to a high critical density, being to some extent obstructive to transmission, are comparatively ineffective in restraining the incidence of the disease should that level be exceeded. One would expect low endemicities to be common when malaria is carried by



mosquitoes which are short-lived or feed relatively rarely on man, but high endemicities should not be an extreme rarity, being in fact easily attained.

The idea of sensitivity concerns the degree to which the endemic level is altered by a change in one of the controlling factors. Its analysis is rewarding, and valuable epidemiological deductions from it do not depend on exact numerical assessment of the values of the factors involved, but more on a realization of their order of magnitude. It is analysed mathematically by the production of partial derivatives of the expression for the endemic level with reference to each of the factors. These partial derivatives are set out in expressions (18), (20), (21), (22) and (23), with a modification of the first to conform with normal practice in expression (19), which regards increase in anopheline numbers as proportional to the original values and not as merely additive. An effort will be made to give their significance individually, though the turning of symbols into words inevitably involves turning precision into vagueness, but the real significance is better seen in the discussion of epidemiological types which follows and is largely based on the derivatives.

In this context a partial derivative is the ratio of the change in the endemic level to a change in one of the factors which influence it, and obviously the ratio should be taken for each of the factors *separately*, to see how sensitive the level is to changes in mosquito density, mosquito longevity, anthropophilism, etc. It is a ratio in the simple sense of the word; if one takes expression (21) and finds that the numerical value of the right side is 0.2, it means that an increase of one day in the extrinsic cycle will result in a fall of 0.2 (20 per cent.) in the endemic level. The change is inverse because the derivative is negative in sign, the logarithm of a fraction always being negative.

From what has been said above on the way in which progressive multiplication is curbed one would expect both the proportion of infected people and the longevity and man-biting habits of the mosquito to influence the sensitivity, making it more marked when they are low and *vice versa*. In fact all the partial derivatives contain the subsidiary expression:  $L - \frac{\log_e p}{a}$  which is a precise

statement of this expectation. It relates sensitivity to the pre-existing endemic level and to the average number of feeds on man which a mosquito takes in the course of its life-time. Applying rough numerical values for the sake of illustration, one might suggest that this last varies from about 5 for *A. gambiae* to 0.025 in the case of *A. culicifacies* in Madras, and that the malaria carried by the latter is therefore a couple of hundred times as sensitive as malaria carried by the former.

This subordinate expression gives the theme of all the partial derivatives, but the detail of some of them varies from it. When the factor which changes is mosquito density and one looks on the change as proportionate to the original density (19), the general theme is unaltered. It is worth noting that it contains no element of duration of the extrinsic cycle, or of the recovery rate, which means that though these influence the endemic level, they do not influence the stability of equilibrium of that level in relation to changes in mosquito density. The statistical demonstration by SWAROOP (1949) that Punjab epidemics are just as likely to occur in places where the spleen rate is high as in those where it is low is relevant.

When the factor which is liable to change is either mosquito longevity, or duration of the extrinsic cycle, or anthropophilism (expressions 20, 21 and 22), the influence of a short life in making the level more sensitive to changes is considerably exaggerated beyond the general theme, though in a different way in each case. It is also notable that the duration of the extrinsic cycle enters into the formation of the first two of these expressions, in a way which means that when it is long the sensitivity is greatly increased. One would



therefore expect high-altitude malaria to be much more liable to fluctuate in response to changes in the length of mosquito life than similar malaria at a low altitude, and this seems to be probably the case in Africa. Similarly malaria transmitted by zoophilic mosquitoes should be brought to an end much more readily by cool weather than that carried by anthropophilic mosquitoes, but should occur as abrupt epidemics when temperature makes its transmission possible. There is also included in the Appendix an expression for sensitivity to changes in the recovery rate (23), which follows the general theme but also varies inversely with the pre-existing recovery rate. This rate is not liable to abrupt change, or to any change except as an aftermath to other events, and its significance in this context is therefore slight.

### Epidemiological Types

The implications of these expressions for critical densities, endemic level and sensitivity are numerous and definite. From them it is possible to describe in detail the epidemiology of two types of malaria representing the two ends of the scale of stability and instability. The descriptions of these types which follow are derived exclusively from the mathematical expressions, except that the statements on immunity are logical deductions from the other statements and are not independently derived. The test of their veracity lies in the degree to which they correspond with natural happenings, which will be discussed in a later section.

#### Stable Malaria

*Determining causes.*—Transmission by a vector with a frequent man-biting habit, with a moderate to high longevity, at a temperature favourable to rapid completion of the extrinsic cycle.

*Anopheline density needed to maintain transmission.*—Very low, of the order of 0.025 bite on the average person each night, or even less.

*Endemicity.*—Anophelism without malaria would probably be unknown. Low to moderate endemicities would probably be found, but very high endemicities would be common.

*Seasonal changes.*—Reduction of temperature below about 15°C. would stop transmission, a seasonal epidemic occurring during the warm weather, starting at a relatively low temperature and only terminated by low temperature. Seasonal conditions unfavourable to breeding or to prolonged adult survival would not be likely to terminate transmission completely unless the reduction of breeding was extremely marked.

*Fluctuations in incidence.*—Fluctuations other than normal seasonal changes are not likely to be marked except in the presence of obvious causes. Epidemics would be very unlikely to occur.

*Effect of cool weather.*—Transmission is likely to continue at almost all temperatures permitting completion of the extrinsic cycle, and therefore tends to occur at high altitudes and latitudes within the range of the vector. In cool weather the sensitivity to changes in probability of mosquito survival becomes exaggerated, so that marked fluctuations and epidemics might occur in such places. Sensitivity to changes in anopheline density remains materially unaltered by cool weather.

*Immunity of population.*—The regularity of transmission is likely to ensure a stable immunity, varying in degree from place to place, but all except the youngest children will have some experience of malaria and resistance to it.

*Amenability to control.*—Very difficult to control. Control by prevention of breeding would not be effective unless near-perfection is achieved, transmission continuing in the presence of very small residual breeding. Control



by imagocides would be relatively difficult, to be effective needing the achievement of a 40 or 50 per cent. daily mortality among the vectors. Control falling only slightly short of the necessary quality is not likely to produce much apparent result. The "wearing out" of imagocidal control would be apparent at an early stage and would produce epidemics which would be severe but not necessarily abrupt in their timing.

### **Unstable Malaria**

*Determining causes.*—Transmission by a vector which bites man relatively infrequently. If the vector is short-lived, or the temperature unfavourable to rapid completion of the extrinsic cycle, the characteristics of the type would be exaggerated. These last two factors alone, without the rarity of feeding on man, would produce an intermediate type between this and stable malaria.

*Anopheline density needed to maintain transmission.*—Relatively high, of the order of 1 to 10 or even more bites on each person each night.

*Endemicity.*—Anophelism without malaria would probably occur in some localities, perhaps over considerable areas, as a result of breeding being insufficient to maintain the high densities needed for transmission. In other places low to moderate endemicities would occur but would not necessarily predominate. High endemicities might be common.

*Seasonal changes.*—Likely to be very marked, in response to temperature changes, unfavourable breeding conditions or dryness of the atmosphere. Seasonal epidemics would not be likely to occur till the temperature is relatively high, and would be likely to be brought quickly to an end by a drop in temperature. Seasonal epidemics would be very abrupt and severe when they do occur, despite their late appearance.

*Fluctuations in incidence.*—Likely to be very marked; at times they would be due to causes so small as to be inapparent except on close study. They might take all forms, such as exaggerated seasonal epidemics, exacerbations of endemicity, or major regional epidemics, the first two tending to follow increase in breeding conditions, the last some climatic factor increasing longevity or breeding over a large area. Equivalent reductions in local or general incidence could occur. The invasion of previously non-malarial areas by the disease and the reversion of malarious places to a non-malarious character are other aspects of the same fluctuation.

*Effect of cool weather.*—Cool weather would rapidly bring this type of malaria to an end. Mosquitoes biting man infrequently could not maintain malaria at high altitudes or latitudes. Transmission in summer-winter climates would be limited to the hot part of summer, starting late and ending early, but epidemics might be severe within this limited time.

*Immunity of the population.*—As a result of the fluctuations in endemicity, and not as their cause, immunity would be very variable. Circumstances could readily arise in which a notable part of the child population had a negligible experience of malaria in places commonly regarded as definitely malarious.

*Amenability to control.*—Controlled with much more ease than stable malaria. Moderate efficiency in prevention of breeding should be effective and control by imagocides is likely to be very easy, mortalities such as 20 to 25 per cent. daily often being sufficient. Control falling short of the desired degree would produce little apparent improvement; the "wearing out" of imagocidal control would not be apparent until a late stage but when this stage was reached would produce epidemics which would be both severe and abrupt in their timing.

### **Epidemic Malaria**

Epidemic malaria may be caused by an increase in anopheline density, in the probability of anopheline survival, or in the frequency of biting man;



or by a decrease in the period of the extrinsic cycle. Its manifestations are likely to be greatly restricted by the development of a firm immunity in the population. Changes of very small degree in the factors mentioned will cause a great increase in the amount of transmission in the circumstances described as determining unstable malaria. The probable happening where malaria is unstable is that the amount of transmission fluctuates greatly from year to year round a mean value. If this mean value is sufficiently high the downward movement may rarely lead to virtual cessation of transmission. In this case the entire population, including the child population, would always have had some experience of malaria and so have sufficient resistance to the toxic manifestations, at least of epidemics.

If the mean value is only moderately high, or is low, the downward fluctuations might lead to virtual cessation of transmission in some years and so leave a material part of the population without experience of malaria and without the ability to resist the effects of the subsequent inevitable upward swing of transmission under unstable conditions.

An epidemic requires a material time for its development. The timing is not here considered in detail, but it seems probable that the development of a full epidemic is only possible when transmission at the enhanced rate continues for at least three times the combined incubation period of malaria in the mosquito and in man to the time of appearance of infective gametocytes. Sufficient time must therefore be added to the other circumstances necessary for epidemic production, and in some cases a prolongation of time of transmission beyond the normal might permit the development of an epidemic without change from normal in the other factors.

The essential causation of epidemics, it is suggested, is usually the transmission of the disease by insects which normally bite man relatively rarely or are short-lived, or transmission in cool climates, which produces the same results in some degree whatever the nature of the vector. An alternative cause is climatic variation which causes the time during which the critical density of anophelines is exceeded to vary materially. This is very much more likely to occur when the critical density is high, under the influence of the factors which cause instability, and so is merely another aspect of the same characteristic. The low immunity encountered in inter-epidemic times is a manifestation of the fluctuating transmission due to instability and not a controlling factor in it.

### Comparison of Theory with Nature

No attempt will be made at a universal comparison ; it will be limited to a few species, selected because the author has personal experience of them and the data available are sufficient basis for statement. The anthropophilism of a species varies from place to place, though when the variations are marked it is probable that the species is essentially zoophilic and only turns to man as a main source of food as an alternative to starvation, or that distinct biological races exist. The probability of survival also changes from time to time, and a mosquito which has typically had a very short life may become long-lived when climatic conditions are favourable to it. For the present purpose it is necessary to consider the normal characteristics of the vector during the bulk of the time it is transmitting malaria in the locality concerned, variations from which may constitute cause for outbreaks, or for diminution of the disease.

The epidemiology of malaria as carried by *A. gambiae*, *A. funestus*, *A. minimus*, *A. fluviatilis* (in South India), and *A. sacharovi*, seems to correspond closely with the type described as stable malaria. Although the author has no personal experience of them, he thinks that the types of malaria transmitted by *A. sundanicus*, *A. leucosphyrus*, *A. varuna*, *A. hyrcanus* var. *sinensis* and *A. atroparvus* have an epidemiology of the same essential form. The detail



of *A. gambiae* malaria will be sufficient illustration ; in discussing it and the malaria carried by *A. culicifacies* (below) : the scheme of description used in the preceding section on epidemiological types will be closely followed.

*A. gambiae* appears to be highly anthropophilic (SYMES, 1932 *a* and *b*, KAUNTZE and SYMES, 1933, DE MEILLON, 1951) though the last author suggests that it may be zoophilic in the extremes of its range. The sporozoite rates commonly recorded in coastal equatorial Africa are only explicable on the basis of both a high anthropophilic index and a high longevity (MACDONALD, 1952). The normal mean temperature of that region is about 26°C., which probably permits the completion of the extrinsic cycle of *Plasmodium falciparum* in 12 days. The critical density is certainly below 0.029, as WALTON (1947) showed that this mean density permitted the continued transmission of malaria. Anophelism without malaria has not been recorded. Very high endemicities are extremely common, but are not invariable. Seasonal changes other than temperature changes alter the amount of transmission, but rarely bring it to a complete end, entirely non-malarious seasons during the warm weather being very rare. In those places where there is a winter the picture is complicated by cessation of breeding, but it seems that transmission starts soon after the advent of suitable temperature. Within the equatorial zone at low levels the stability of malaria carried by *A. gambiae* is well known and acknowledged, marked changes from year to year being almost unknown. Within this zone there is no recorded epidemic tendency. The disease occurs at high altitudes, reaching 6,000 feet and sometimes greater heights. Epidemics occur at these high altitudes (GARNHAM, 1945) and at the extremes of its distribution (DE MEILLON, 1951). The epidemics at high altitudes are attributed mainly to variations in the probability of survival (WILSON, 1949) and DE MEILLON (*loc. cit.*) considers that *A. gambiae* may be zoophilic in these areas ; the evidence is not convincing, but if it were, it would give additional explanation of the epidemics. The studies of WILSON (1936, 1938, 1939, 1949) which show the common acquisition of considerable resistance to infection, are well known, and though the present writer disputes some deductions from it he does not dispute the essential fact. The difficulty of control by prevention of breeding is well established, and is illustrated by WALTON (1947). Control by imogicides has had a variable degree of success.

Malaria carried by *A. culicifacies*, *A. stephensi*, *A. philippinensis* and *A. superpictus* closely resembles the description of unstable malaria. Although he has no personal experience of them, the present writer thinks that the epidemiologies of malaria carried by the following anophelines also conform to this general description : *A. maculatus*, *A. aconitus*, *A. annularis*, *A. punctulatus*, *A. minimus* var. *flaviviridis*, *A. albimanus* and *A. aquasalis*.

*A. culicifacies* malaria will be given as a sole example. The species is zoophilic but may feed predominantly on man when insufficient animal food is available (RUSSELL and RAO, 1942 *a* ; RUSSELL and JACOB, 1939 ; COVELL, 1944 ; SENIOR WHITE, 1947). Over long seasons of malaria transmission it is typically very short-lived, but when suitable climatic conditions, which are rather cool, occur it may be long-lived (AFRIDI *et al.*, 1940). The summer temperature over most of its range is hot enough to permit rapid completion of the extrinsic cycle. The critical density is high, represented in Madras by catches of between 7-10 and 17-20 per man-hour, but it is probably considerably lower elsewhere, as there is evidence that the extremely low anthropophilic indices and longevity recorded in Madras are below the average. Anophelism without malaria is well known (RUSSELL and RAO, 1942 *b*). In malarious localities high endemicities are quite common—a large part of Ceylon was hyperendemic until controlled—but low endemicities are also common. The occurrence of seasonal variations in response to factors other



than temperature change is very marked. Different parts of Ceylon experience quite different seasons owing to differences in season of rain or humidity which are not themselves always marked, in fact the physical or climatic differences between neighbouring non-malarious and highly malarious areas are often very difficult to discern. Seasonal epidemics are typically very abrupt. Fluctuations in incidence are extremely marked. There are well known epidemic areas in the Punjab and Ceylon, less well known ones in the Central Provinces of India and in Travancore, and CHRISTOPHERS and SINTON (1926) describe the epidemiology of malaria over a very large part of its range as being liable to fluctuations. It does not occur at any considerable altitude, normally ending between 2,000 and 3,000 feet above sea level, but the validity of this as evidence is marred by the fact that this is near the upper limit of breeding. The insecure immunity of the population in areas subject to this malaria has been described by GILL (*loc. cit.*). Personal experience shows that it is more amenable to control by prevention of breeding than malaria carried by either *A. minimus* or *A. gambiae*. Control by imagocides has been brilliantly successful in a number of places, especially Ceylon (RAJENDRAM and JAYEWICKREME, 1951).

In contrast to *A. culicifacies* another supposed member of this group, *A. superpictus*, occurs at relatively high altitudes. It is an important vector in Cyprus and in the lowlands of Syria and the Lebanon, where it causes very abrupt outbreaks which start later in the year than those caused by the anthropophilic *A. sacharovi*, and end earlier. Though an extremely potent carrier in these places it ceases to act as a vector in the mountains of the Lebanon at an altitude of 1,000 feet below that at which *A. sacharovi* ceases to carry. In the cooler climates of northern Greece it is not an important vector (BARBER and RICE, 1935).

*A. pharoensis* in Egypt represents an intermediate type, being highly anthropophilic (BARBER, 1936), and the evidence of comparative oöcyst and sporozoite rates suggests that it is very short-lived (MACDONALD, 1952). The malaria it carries has an intermediate character, being relatively stable though with marked variations in severity from place to place. There is insufficient valid evidence on which to support a firm statement, but the author suspects that *A. quadrimaculatus* and *A. darlingi* have similar characteristics.

According to the statement of epidemiological types malaria can only be maintained at high altitudes and in other cool climates by anthropophilic mosquitoes which, in warmer climates, would convey a stable variety of the disease. The influence of cold, however, would be to lessen this stability and make periodical fluctuations greater. HACKETT (1945) discusses high altitude malaria with particular reference to the Andes where it is transmitted by *A. pseudopunctipennis*, and with lesser reference to Africa and the highlands of the Burmese hinterland. It is clear from the work of DAVIS and SHANNON (1928), CORRADETTI (1948) and VARGAS (1938, quoted by BOYD, 1949) that *A. pseudopunctipennis* is highly anthropophilic in its Andean distribution, though it is zoophilic in other parts of its range such as in Venezuela, as shown by HILL (1934). The high altitude malaria of Africa is transmitted by *A. gambiae*, the characteristics of which have already been mentioned. Malaria in Yunnan on the Burma-China road has been described by WILLIAMS (1941) as occurring up to an altitude of 6,000 feet and is transmitted by *A. minimus*. This mosquito has already been referred to as a highly anthropophilic species carrying stable malaria at lower altitudes.

### Discussion

Mathematical theory suggests the classification of malaria according to the habits of the vector into two types, representing the ends of a continuous range,



which have been described as stable and unstable malaria. These two types have been elaborated in some detail, and they bring together a number of epidemiological characteristics which have not previously been related to each other, and which here seem to fall into logical connexion. They relate several epidemiological features to a limited number of mosquito characteristics and to the period of the extrinsic cycle. They relate them in a way which seems to coincide closely with happenings in nature over a large part of the world, and present an integrated picture in exchange for a multitude of unrelated facts which, of necessity, have composed the usual epidemiological picture of malaria. In particular they apply a rational explanation of epidemic potential which could well explain the differences in periodic happenings observed in different parts of the world, and they associate this with other natural differences such as amenability to control, the effects of altitude and degree of endemicity.

Two examples of the natural epidemiology have been described and they seem to correspond closely with the types described on a basis of reasoning, and, so far as the author's knowledge goes, the general epidemiology of malaria also agrees with the types described. There therefore seem to be reasonable *prima facie* grounds for accepting the theoretical description as representing the fundamental epidemiology of the disease.

The description has been developed in the context of malaria, but the primary reasoning is of a type which refers to any disease which is carried from man to man by an insect, provided that it is of a type in which superinfection of man can occur. It similarly applies to transmission of such diseases among other animals but not without modification to those in which two species of mammalian host are concerned. The group to which it refers probably includes most of the protozoal and helminthic diseases carried by arthropods. The various diseases which confer immunity would need separate examination, though it might well turn out that their epidemiology was similar in form.

The primary classification of malaria in the past has been on a basis of endemicity, the last groupings proposed being those of the Kampala Conference (W.H.O., 1951) which classified endemicities as holo-endemic, hyper-endemic, meso-endemic and hypo-endemic. Subsidiary classifications have been made under these headings and one of the principal ones has been by epidemic potential or "constitution" (GABALDON, 1949); others have been by such criteria as length of season, altitude, etc. It is now suggested that the proper primary classification of malaria is into the two types, stable and unstable, on a basis of the normal characteristics of the vector during the malaria season, or on the observed nature of the epidemiology, and that other classifications should be subordinate to this. Very highly endemic malaria could occur in places where the constitution is unstable as, for instance, in Ceylon, but its general characteristics are decided more by the instability than by the high endemicity. Much of the existing conflict about the facts of hyper- or holo-endemic malaria could be resolved if the distinction were between stability and instability rather than between hyper-endemicity and supposedly low endemicity. Though discussion on the process of immunization would continue, the predictability of a firm resistance in the one case, and its uncertainty in the other, would be explained. Similarly the differences which have been encountered in the success of control in equatorial Africa and in the previously hyper-endemic parts of Ceylon and other places could be understood.

Some of the apparent inconsistencies of malaria in labour forces could also be explained by this classification. The epidemic tendency among labour forces in some parts of the world is extreme and notorious, while in others such as East Africa it is often a minor characteristic. The mixture of immune and non-immune peoples and the introduction of new strains of parasite have always seemed to the writer to be inadequate explanations of happenings.



They probably play a part, but the separation of a cattle-owning people from their cattle in the presence of a predominantly zoophilic anopheline may well play a larger one and, as an illustration of the extreme sensitivity of malaria carried by such anophelines, lead to great epidemics.

On this basis the following description is put forward as the fundamental epidemiology of malaria, and of any disease which is carried from man to man by arthropods and in which superinfection occurs: the essential factors are the duration of the extrinsic cycle of the parasite, the frequency with which the vector feeds on man, and the vector's normal longevity. These last two can be related to each other as the average number of feeds on man which the insect takes during its life-time.

These factors act in two ways which are converse to each other. They affect the probability of an insect becoming infected and thus the density of insects needed to maintain continuous transmission. If, however, this density is exceeded they influence in an opposite way the probability of two or more infections in the insect masking all but one, and so curbing the progressive multiplication of human cases.

By their first action they determine the critical density of insects in relation to man, below which the disease tends to disappear. Their second action when the critical density is exceeded determines the stability of the disease. By the combined influence of the two actions they decide within the geographical range of the insect the seasonal and spatial distribution of the disease, its endemicity, its liability to fluctuations, the consequent immune reactions of the people and the amenability of the disease to control. These characteristics are influenced together, in the manner described in the text under the heading *Epidemiological Types*, and according to the degree of the controlling factors the epidemiology of the resultant malaria corresponds to some point in the scale between the extremes described as stable and unstable malaria. The general epidemiological features of the disease are determined more by the degree of stability than by the degree of endemicity which results, though there is a partial relation between the two.

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### Summary

The methods of study of malaria of high epidemic potential and the more stable disease are briefly reviewed, together with opinion on the causation of instability and stability. The current opinion that instability is due to interruption of transmission and consequent fluctuations in immunity is stated; it is accepted as a sound explanation of what happens under unstable conditions, but not as a reason for its happening. It is pointed out that it provides no explanation for the gross variations in the amount of transmission which are in fact the basic cause of instability.

The theory of equilibrium is elaborated by mathematical argument in an appendix, and by a verbal explanation inserted in the text. It includes a statement of the critical density of anophelines, of the mechanism of establishment of the endemic level in the population, and of the sensitivity of the equilibrium of this endemic level to changes in the factors which influence it. This theory shows that an infrequent man-biting habit on the part of the vector, a short average length of life, or a long extrinsic cycle of the parasite, must lead



to a high critical density. If, however, this critical density is exceeded, these characteristics have a much smaller effect in restraining the endemic level, and lead to the production of an extremely unstable disease, the equilibrium of which is very readily upset. The reasons for this, and some details of it, are set out.

On the basis of mathematical argument two epidemiological types of malaria are described under the headings :—determining causes ; anopheline density needed to maintain transmission ; endemicity ; seasonal changes ; fluctuations in incidence ; effect of cool weather ; immunity of population ; and amenability to control. This argument is elaborated by a statement of the mechanism of causation of epidemics in the unstable type.

A comparison is made with natural happenings, in which the malarias transmitted by *A. gambiae* and *A. culicifacies* are selected to represent the stable and unstable types, their epidemiology being described under the headings mentioned above. A number of other notorious vectors are named and the correspondence of the malaria they carry to one or other of the types is indicated.

It is concluded that the classification of malaria by stability or instability, according to the characteristics of the vectors, provides a more integrated picture of the epidemiology of the disease than has been presented by any other methods. In particular it relates a considerable number of common epidemiological features to a few mosquito characteristics in a way which both accords with mathematical reasoning and corresponds with happenings in nature. It is therefore thought that the explanations provided constitute the fundamental epidemiology of the disease, and of other diseases carried from man to man by insects, and in which superinfection of man is possible.

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## Appendix

### *Mathematical Argument*

#### *Symbols*

Symbols are used with the following meanings :—

- m* the anopheline density in relation to man.
- a* the average number of men bitten by one mosquito in one day.
- b* the proportion of those anophelines with sporozoites in their glands which are actually infective.
- p* the probability of a mosquito surviving through one whole day.
- n* the time taken for completion of the extrinsic cycle.
- s* the proportion of mosquitoes with sporozoites in their salivary glands.
- h* the proportion of the population receiving infective inocula in one day.
- x* the proportion of people affected (that is showing parasitaemia).
- L* the limiting value of the proportion of men infected when equilibrium is reached.
- r* the proportion of affected people, who have received one infective inoculum only, who revert to the unaffected state in one day.
- t* time in days.
- e* the base of natural logarithms, 2.71828.



Expressions already established (MACDONALD, 1950 a, b, 1952)

When  $h$  is constant, and does not exceed  $r$  :—

$$\frac{dx}{dt} = h - rx \quad \dots \quad \dots \quad \dots \quad \dots \quad (1)$$

$$L = \frac{h}{r} \quad \dots \quad \dots \quad \dots \quad \dots \quad (2)$$

$$x = L - (L - x_0)e^{-rt} \quad \dots \quad \dots \quad \dots \quad (3)$$

When  $h$  is constant, and equals or exceeds  $r$  :—

$$\frac{dx}{dt} = h(1 - x) \quad \dots \quad \dots \quad \dots \quad \dots \quad (4)$$

$$L = 1.0 \quad \dots \quad \dots \quad \dots \quad \dots \quad (5)$$

$$x = 1 - (1 - x_0)e^{-ht} \quad \dots \quad \dots \quad \dots \quad (6)$$

A mosquito's expectation of life is :—

$$\frac{1}{-\log_e p} \quad \dots \quad \dots \quad \dots \quad \dots \quad (7)$$

A mosquito's expectation of life after survival through  $n$  days is :—

$$\frac{p^n}{-\log_e p} \quad \dots \quad \dots \quad \dots \quad \dots \quad (8)$$

The sporozoite rate,  $s$ , is :—

$$\frac{p^n ax}{ax - \log_e p} \quad \dots \quad \dots \quad \dots \quad \dots \quad (9)$$

### Basic Reproduction Rate of Malaria

*Definition.*—The number of infections distributed in a community as the direct result of the presence in it of a single primary non-immune case.

The primary case would be infective for  $\frac{1}{v}$  days, on each of which he would be bitten by  $ma$  mosquitoes, each with an expectation of life after survival through  $n$  days of :—

$$\frac{p^n}{-\log_e p} \quad \dots \quad \dots \quad \dots \quad \dots \quad (\text{see } 8)$$

Each would bite man an average of  $a$  times on each day of its survival, and since the proportion of these bites which would be infective is  $b$  it follows that the total number of infections distributed would be :—

$$\frac{ma^2bp^n}{-r \log_e p} \quad \dots \quad \dots \quad \dots \quad \dots \quad (10)$$

### The Endemic Level

*Definition.*—The proportion of the population affected when stability is reached, and before the common acquisition of material resistance.

The inoculation rate, or proportion of the population receiving infective inocula on one day, is expressed by :—

$$h = mabs \quad \dots \quad \dots \quad \dots \quad \dots \quad (11)$$

in which the full expression for  $s$  may be inserted to read :—

$$h = \frac{ma^2bxp^n}{ax - \log_e p} \quad \dots \quad \dots \quad \dots \quad \dots \quad (12)$$



and when  $h$  does not exceed  $r$  :—

$$\frac{dx_2}{dt} = \frac{ma^2bx_1p^n}{ax_1 - \log_e p} - rx_2 \quad \dots \quad \dots \quad \dots \quad (13)$$

in which the forms  $x_1$  and  $x_2$  are used to indicate that they refer to values of  $x$  at different times, separated by the time interval of the incubation period in the mosquito *plus* that in man. When the limit of this expression is considered, this is immaterial because at that time  $x_2$  and  $x_1$  are by definition the same.

When  $h$  equals or exceeds  $r$  :—

$$\frac{dx_2}{dt} = \frac{ma^2bx_1p^n(1 - x_2)}{ax_1 - \log_e p} \quad \dots \quad \dots \quad \dots \quad (14)$$

The first of these has two limits, a finite one when :—

$$L_x = \frac{mabp^n}{r} + \frac{\log_e p}{a} \quad \dots \quad \dots \quad \dots \quad (15)$$

and also a limit of zero. The limit is attained when :—

$$\frac{ax - \log_e p}{mp^n} = \frac{a^2b}{r} \quad \dots \quad \dots \quad \dots \quad \dots \quad (16)$$

This can be turned to give an explicit value of  $m$  for a constant known value of  $p$ , or an implicit value of  $p$  for constant known values of  $m$ .

The second differential has a theoretical zero limit which is, however, incompatible with the prerequisite that  $h$  should equal or exceed  $r$  to make it operative, and a sole effective limit of 1.0.

### *The Critical Density*

*Definition.*—The greatest density of mosquitoes, in relation to the numbers of people, affecting any community, which will result in the progressive reduction of malaria to an utterly negligible level, it being assumed that the probability of a mosquito surviving through one day is constant and known.

The level is given by the explicit value of  $m$  for the zero limit of the first differential given above. It is :—

$$m = \frac{-r \log_e p}{a^2bp^n} \quad \dots \quad \dots \quad \dots \quad \dots \quad (17)$$

This is in effect the same as the critical level of Ross.

### *Indices of Sensitivity*

*Definition.*—An index of sensitivity is the ratio of the increase in the endemic level, between the values zero and 1.0, to an increase in one of the factors which influence it.

The indices are basically the partial derivatives of  $L$  with reference to one of the other factors. As, however, increase of mosquito density, or mosquito breeding, is commonly and properly regarded as a proportionate increase relative to its previous value, the corresponding derivative (18) has been modified to correspond with this. The primary derivatives are all modified by substitution of equivalent values for  $p^n$ , or  $m$ , derived from the parent expression, to give them a common form.

i. In relation to changes in mosquito density :—

$$\begin{aligned} \frac{\partial L}{\partial m} &= \frac{abp^n}{r} \\ &= \frac{La - \log_e p}{ma} \quad \dots \quad \dots \quad \dots \quad \dots \quad (18) \end{aligned}$$

which is modified to show the ratio of increase in  $L$  corresponding to a multiplication in  $m$ , to give an index of :—

$$L = \frac{\log_e p}{a} \dots \dots \dots (19)$$

ii. In relation to changes in probability of mosquito survival :—

$$\begin{aligned} \frac{\partial L}{\partial p} &= \frac{mabnp^{n-1}}{r} + \frac{1}{ap} \\ &= \frac{n(La - \log_e p) + 1}{ap} \dots \dots \dots (20) \end{aligned}$$

iii. In relation to changes in the period of the extrinsic cycle :—

$$\begin{aligned} \frac{\partial L}{\partial n} &= \frac{p^n \log_e p \cdot mab}{r} \\ &= \log_e p \left( L - \frac{\log_e p}{a} \right) \dots \dots \dots (21) \end{aligned}$$

(N.B.—This expression has a negative value.)

iv. In relation to changes in the man-biting habit :—

$$\begin{aligned} \frac{\partial L}{\partial a} &= \frac{mbp^n}{r} - \frac{\log_e p}{a^2} \\ &= \frac{La - 2 \log_e p}{a^2} \dots \dots \dots (22) \end{aligned}$$

v. In relation to changes in the rate of recovery :—

$$\begin{aligned} \frac{\partial L}{\partial r} &= - \frac{mabp^n}{r^2} \\ &= - \frac{1}{r} \left( L - \frac{\log_e p}{a} \right) \dots \dots \dots (23) \end{aligned}$$

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## SUMMARY OF RECENT ABSTRACTS\*

## VII. HELMINTHIASIS

*(Continued from p. 749)*

## NEMATODES

*General*

Various surveys have been reported. In Portugal no less than 88 per cent. of 910 recruits had some worm infection, including *Ascaris* (67 per cent.), and hookworms (23) (MAIA, p. 377). In Germans and other people in the Balkans during the war the commonest worms were *Ascaris* and *Trichuris* (ERHARDT, p. 899), and in Warsaw *Trichuris* and *Enterobius* (JANICKI *et al.*, p. 900). Hookworm infection is rare on one of the Cape Verde Islands, but NOGUEIRA and COITO (p. 384) found mild infection in 37 per cent. of people on another. *Trichuris* and *Ascaris* were more prevalent.

*Hookworm Infection, Strongyloides, etc.*

COUTELEN (p. 745) shows that miners have been engaged in northern France who are carriers of hookworms. Some were Italians who had done agricultural work, some Frenchmen from Indo-China. Symptoms were slight. To avoid the risk of transmission all applicants for work should be examined systematically. Hookworm infection is found in 34 per cent. of adults in part of the Province of Genoa, mostly in workers in metal mines. *Ascaris* and other worms are also common (PETRILLI, p. 56).

Coal miners in India show high hookworm rates, especially the underground workers. MUKERJI and MATHEN (p. 174) found the rates also high in the age-group 16-20, in females, in those living in colliery quarters, and in those who had recently come to the mines; they were low in those who used latrines and in clerks. There were great differences between different collieries.

Agricultural workers also show high rates. The infection is common in vegetable growers near Madrid (MATILLA *et al.*, p. 662). In the Province of Szechwan, W. China, the infection rate, worm load, and incidence of anaemia and clinical disease are all high, especially where sweet potato and corn are inter-cropped, but rice cultivation is not favourable to the infection. CHANG *et al.* (p. 275) show that human faeces are much used as fertilizer and it is not feasible to disinfect them, though it may be possible to reduce contact with infected soil by modifying the method of transplanting sweet potato.

MATILLA *et al.* (p. 573) report a case in which symptoms resembling those of carcinoma of the stomach were apparently due to hookworm infection.

Studies on hookworm anaemia are reported by HAHN and OFFUTT (p. 175), who have devised a method for studying blood loss by using radio-active iron in dogs. BENETAZZO and GAMBINI (p. 277), think that there is no toxic element, but that the anaemia is due to blood loss and iron deficiency. If the bone marrow becomes functionally exhausted the anaemia may persist after the worms are expelled, but iron in large doses may relieve it even if anthelmintics are not given. This last statement is not, in the opinion of CARVALHO *et al.* (p.

\*The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1951, v. 48. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.



1136), always correct, and they quote cases in children to illustrate their point. MATILLA *et al.* (p. 822) regard the anaemia as hypochromic, due to poverty in iron, and LARIZZA and VENTURA (p. 1135) take a similar view in their monograph on the subject. They note that although hookworm infection is being reduced in miners in Italy, it is increasing in land workers.

In a paper on the worms passed by residents in various places in Brazil, after treatment with hexylresorcinol, DEANE (p. 818) notes that this drug appears to be much more effective against *Necator* than against *Ancylostoma*.

EICHBAUM *et al.* (p. 1023) report on the action of cashew-nut oil in hookworm infection, but in comment Napier states that the results obtained were not as good as would be expected from hexylresorcinol or tetrachlorethylene.

The present tendency in hookworm control programmes in the United States is to concentrate on infected families rather than on infected individuals, and to identify these families by a special form of survey in which hookworm disease rather than hookworm infection is sought. BEAVER (p. 903) shows that surveys based on egg counts restricted to anaemic persons will discover most of the extremely heavy infections, but may miss an important group whose haemoglobin levels, though reduced by hookworm infection, are still within the normal range.

BROCCA (p. 1024) has established differences between *Ancylostoma braziliense* and *A. ceylanicum*, and states that though the latter is a relatively frequent parasite of man, there is doubt whether *A. braziliense* has ever infected man.

HORTON (p. 277) reports some success in the treatment of creeping eruption with hetrazan.

GALLIARD (p. 1024) discusses experimental infection with *Strongyloides stercoralis* in Tonking, and the effect of therapeutic agents on the parasitic worms, and of physical and chemical factors on the free-living forms.

#### *Ascaris, etc.*

Eggs of *Enterobius* and *Ascaris* have been found on paper money by SCHMIDT *et al.* (p. 62) in Germany, where much attention has been given to the subject of transmission of *Ascaris*, the incidence of which has been increasing in some parts, for instance Thuringia where human faeces are used in market gardens (LOMMEL, p. 904). The use of sewage for fertilization and the risk of helminthiasis are discussed by SEISER (p. 567), and LEGLER (p. 663) has devised a method of counting *Ascaris* eggs in sewage effluent, and in faeces, which involves microscopic examination of a membrane (or filter paper) through which the fluid is passed. Most *Ascaris* eggs in sewage are destroyed in the various processes in Stuttgart, however, and SCHMIDT and WIELAND (p. 176) conclude that transmission to man is not possible. On the other hand, GÄRTNER and MÜTING (p. 486) show that *Ascaris* eggs in sewage spread on to soil can be found 11 months later to a depth of 30 cm. They (p. 904) find that eggs in the upper layers are destroyed by sunlight but that in the deeper layers they may persist for more than one year in spite of the injurious anaerobic conditions. In S. Africa similar work by HOGG (p. 58) and by KELLER and HIDE (p. 824) led to similar findings that sunlight and desiccation inactivate the eggs near the surface in a short time. On the other hand the eggs may remain viable after digestion of sewage at mesophilic temperatures and drying on sand beds, and KELLER (p. 487) therefore suggests that sewage should be heated throughout at 54°–55°C. for 2 hours. JETTMAR and EXNER (p. 905) show that though moist heat at 65°C. kills eggs in a few seconds, at 45°C. only half the eggs of *A. megalocéphala* were dead after 7 hours. Dry heat is more effective, and the process of freezing and thawing repeated many times is harmful to the eggs. June sunlight seems to be more effective than August sunlight in Germany.

LEGLER (p. 573) shows that humus in a layer 2.5 cm. thick, and fine sand 3 cm. thick, are efficient in filtering off *Ascaris* eggs from sewage, but MÜLLER (p. 1137) found that the pressure exerted by pumps used in distributing sewage did not harm them.

SANDARS (p. 747) shows that 6 per cent. formalin was not enough to kill *Ascaris* eggs in faeces.

EPPE *et al.* (p. 278) have studied the metabolism of *Ascaris*, and have developed a method of sterilizing them by means of antibiotics. FAIRBAIRN and REESAL (p. 663) have also been able completely to eliminate micro-organisms from the external surface and the intestinal tract of *Ascaris*.

CALLOT and VERMEIL (p. 665) show that eggs of *Ascaris* inserted into the peritoneal cavity of experimental animals do not develop. Eggs of other worms are destroyed by phagocytes in the same conditions, and living *Ascaris* eventually become encapsulated.

SPRENT (p. 823) found that guineapigs infected with larvae or eggs of *Ascaris* (and with *Trichinella*) showed anaphylactic shock when material from whole *Ascaris* was subsequently injected into them. He has investigated the chemical fractions involved and shows that extracts from certain other nematodes produce the same effect. BENETAZZO and ZAMA (p. 385) have used antigens from *Parascaris equorum* for skin and serological tests in persons with various worm infections, but there is doubt as to the specificity of the reactions.

A case of Henoch's purpura due to *Ascaris* is reported by REITANO and FONDACARO (p. 573). In Czechoslovakia the commonest cause of eosinophilic infiltration of the lung is ascariasis (POKORNY and KLAUSOVÁ, p. 177). *Ascaris* infection is almost universal in Syria, and ALTOUNYAN (p. 1025) reports a case of impaction in the common bile duct. A mass due to *Ascaris* larvae attached to the deep muscles of the abdominal wall is described by EL ZAHAWI and OVANESSIONIAN (p. 58).

JELLIFFE (p. 1026) points out the danger of oil of chenopodium when sold to and taken by people who cannot be expected to understand the dosage printed in English on bottles which contain several times the required dose. He quotes 3 cases of fatal poisoning, and suggests that the drug should be sold in packets each containing a single dose (according to age) with magnesium sulphate as a purgative. ETTELDORF and CRAWFORD (p. 486) used hetrazan for *Ascaris* infection, and conclude that in doses of 6 mgm. per kgm. thrice daily for at least a week it will remove *Ascaris* without starvation or purgation.

WENZEL and GIBSON (p. 664) report on the toxicity and anthelmintic activity of *n*-butylidene chloride.

### *Filarial infections*

*Wuchereria bancrofti*.—FAIN (p. 1029) describes 9 adult female and 10 adult male *W. bancrofti* from the Belgian Congo. These are the first descriptions of African specimens.

HUNTINGTON *et al.* (p. 488) discuss filariasis in American troops during the war, arguing that the lymphangitis is an allergic reaction to filarial protein. ABEN-ATHAR (p. 665) similarly regards the pathological process in filariasis as a manifestation of sensitization and local anaphylaxis.

BOWIE (p. 665) reports a heavy incidence of *W. bancrofti* in Nepal, and evidence that *Culex fatigans* is a carrier. This infection had not previously been recorded from Nepal.

BACKHOUSE and HEYDON (p. 386) report observations on filariasis made between 1930 and 1935 at Rabaul. Microfilariae of *W. bancrofti* were found in 19.4–35.1 per cent. of the population of various parts. The microfilariae



show periodicity and are probably transmitted by *Anopheles punctulatus farauti* and *A. p. punctulatus*, but *Aedes scutellaris* is not hospitable to *W. bancrofti* in that area [see correction, p. 1035].

An account of filariasis in Indo-China has been written by CAPPONI (p. 385). CANET (p. 58) has found a high incidence of *W. bancrofti* infection in the indigenous Moïs of Cochín-China. *W. malayi* was not found, though common in neighbouring countries. The chief vector was *Culex fatigans*. HUARD and TRAN ANH (pp. 666, 1030) report on the intradermal test with antigens from *Dirofilaria immitis* in filariasis in Hanoi. They used French and American preparations, and conclude that they are to be relied upon in 60-80 per cent. of cases, but that where possible the complement-fixation test should also be done. HUARD (p. 747) discusses the genital lesions in filariasis in Hanoi, and the operative procedures used in 49 cases.

JACHOWSKI *et al.* (p. 824) calculate, as a result of investigations in Samoa and in Samoans living in Hawaii (where filariasis does not occur) that, in the absence of reinfection, microfilariae of *W. bancrofti* disappear from the blood in a little over 5 years.

In the Report of the Filariasis Research Unit of the East Africa High Commission, LAURIE (p. 1027) shows that the microfilaria rate in different parts varies considerably, the rate being 37 per cent. at one place on Lake Nyasa. Patients with large numbers of microfilariae are more difficult to sterilize with hetrazan than those with smaller numbers. The total maximum dosage should not be less than 70 mgm. per kgm. (*i.e.*, 12 mgm. per kgm. every 12 hours for 3 days). This dose, however, costs 10 shillings per patient. The drug had no effect on microfilariae of *Dipetalonema perstans*.

HAWKING (p. 177) reviews work on filariasis with hetrazan, showing that it acts quickly on the microfilariae of *W. bancrofti* and *O. volvulus*. In *L. carinii* infections of cotton rats the microfilariae after treatment with hetrazan are found mostly in the liver, and are phagocytosed within 18 hours. Hetrazan has little or no action on adult *O. volvulus* and causes severe allergic reactions in that infection; its action on adult *W. bancrofti* is still uncertain. The author states that there is evidence from animal experiments that microfilariae of *W. bancrofti* which show periodicity probably retire to the lungs in the daytime.

PAEZ (p. 1031) reports a case of apparently successful treatment of haematochyluria with hetrazan.

*W. malayi, etc.*—A general account of filariasis in Ceylon, where *W. malayi* is prevalent in rural areas and *W. bancrofti* round Colombo, is given by DASSANAYAKE (p. 487). He refers to the prophylactic value of hetrazan.

POLUNIN (p. 1029) shows that filariasis exists in the interior of the Malay peninsula more widely than previous surveys had indicated, even at an altitude of 1,250-2,800 feet.

BERTRAM (p. 60) has devised a method of calculating the number of *Litomosoides carinii* transmitted to each cotton rat by mites, in experiments on drug treatment.

CANET and JAHAN (p. 180) show that hetrazan had only slight effect on the blood microfilariae of a filaria of dogs.

*Onchocerca*.—NWOKOLO (p. 60) gives an account of onchocerciasis in part of Nigeria, where the dermatitis is the commonest manifestation, with severe pruritus. Ophthalmia was not observed in this series of 100 cases, but 89 nodules were found. The only effective treatment was surgical removal of nodules; hetrazan was not used.

In part of the Gold Coast HUGHES and SARKIES (p. 1031) have found that a long period of exposure is needed before serious manifestations of onchocerciasis appear, but most adults show microfilariae in the skin after 5 years, and 30

per cent. in the eyes after 10 years. Detection of infection, and consequent medical supervision, are possible long before irreversible damage is done to the eyes. The observations were made because of a proposal to build a hydro-electric plant in that area.

PUYUELO (p. 278) found nodules in 10 per cent. and onchocercal blinding in 2.5 per cent. of 88,289 persons examined in the Upper Volta region. Probably many more carried microfilariae in the skin. GEUKENS (p. 825) shows that in part of the Belgian Congo (where *D. perstans* and *L. loa* were also found) the infection rate with *O. volvulus* reaches 100 per cent. in adults, though no evidence of infection could be obtained in children under 6 years. No elephantiasis was found, and eye complications were rare. The chief vector was *Simulium renauxi* n. sp. This species, like *S. neavei*, which is also a vector in the Congo, lives in association with fresh-water crabs, and may in fact be a variety of *S. neavei*. WANSON and HOLEMANS (p. 826) describe the immature stages of these flies. The crabs are found especially in the foamy parts of streams, and larvae and pupae on the ventral surface of the carapace.

VAN SOMEREN and MCMAHON (p. 181) have established that larvae of *Simulium neavei* are found on fresh-water crabs in Kenya.

SARKIES (p. 1043) describes the technique of detection of microfilariae of *O. volvulus* in the aqueous humour of the eye by using an ophthalmoscope incorporating a lens of +20 to +28D. This seems to be more effective than the slit lamp.

TISSEUIL (p. 278) notes that onchocerciasis does not appear to play any part in elephantiasis.

PUYUELO (pp. 182, 908) treated with hetrazan patients suffering from onchocerciasis, and gave them anti-histamine drugs to diminish the allergic reactions. For dosage the original abstract should be consulted. Microfilariae quickly disappeared from the skin, and the clinical condition rapidly improved.

BURCH (p. 576) writes very favourably of suramin in the treatment of onchocerciasis. It does not clear microfilariae so quickly as hetrazan, but the late results appear to be much better. After courses of 8 intravenous injections of 1 gm. at weekly intervals, some 87 per cent. of the patients were free from microfilariae at the end of a year.

*Loa loa*, etc.—KERSHAW (p. 574) has made surveys for *L. loa* and *D. perstans* in West Africa, and finds that examination of 50 cmm. of finger blood as a thick film dehaemoglobinized, fixed and stained with hot Mayer's haemalum, provides a sound basis for these surveys. He has studied the periodicity of *L. loa*, and its relation to the feeding of *Chrysops*. Incidence of *L. loa* infection was 16–23 per cent.

CREWE and O'ROURKE (p. 907) studied the biting habits of *Chrysops silacea* in the forest in the Cameroons. Filarial larvae were found in the flies, but it could not be determined whether they were of human or simian origin.

KENNEY and HEWITT (p. 488) refer to a psychoneurotic syndrome in the course of *L. loa* infection, which disappeared on removal of adult worms or treatment with hetrazan.

WOODRUFF (p. 667) shows that banocide (hetrazan) causes microfilariae of *L. loa* to disappear from the peripheral circulation. At that time microfilariae were found in biopsy material from the liver, and were surrounded by phagocytes. This indicates that the action of the drug is to sensitize the microfilariae, which are then destroyed by phagocytes in the liver [see Hawking above].

*Dracunculus*.—In a village of South-West Nigeria 83 per cent. of the people showed active *Dracunculus* infection in the dry season. ONABAMIRO (p. 1032) shows that the intermediate host was *Thermocyclops nigerianus* and that an infection rate up to 10 per cent. was found in parts of a pond containing this



host, of which only adult females, mostly lacking egg sacs, were infected. In the rainy season active infection in man is much less common, and *Thermocyclops* are comparatively rare.

JELLIFFE (p. 279) describes a case of calcification of a guineaworm.

*Enterobius, Trichuris, Trichinella, etc.*

*Enterobius*.—SCHMIDT and MENDHEIM (p. 183) show that examination of faeces alone is useless in *Enterobius* infection. They found a high rate of infection in children in an orphanage by using a "Cellophane" swab, especially in boys; the dust of the schoolroom contained numerous eggs. TAYLOR and RIDDELL (p. 377) insist that to ensure diagnosis of *Enterobius* infection in children at least 4 stool examinations and 5 NIH swabs, at intervals of 48 hours, are necessary. JEFFERY (p. 184) found the cellulose tape technique more efficient than the "Cellophane" swab in *Enterobius* infections, and notes that tropical conditions do not appear to favour transmission of *Enterobius*.

SCHMIDT *et al.* (p. 577) examine dust for eggs of *Enterobius* by means of adhesive strips which can be pressed on the dusty surface and then examined directly by microscope.

OELKERS (p. 489) has investigated the longevity of *Enterobius* eggs kept under various conditions, for which the original abstract should be consulted. Eggs in the anal region can develop completely to the larval stage in a night, and remain infectious, in dust or on soiled linen, for several weeks. Completely developed eggs are fairly resistant to heat, and those adhering to the skin would not be killed by washing in hot water. They are also resistant to antiseptics, and larvae show considerable resistance to anthelmintics in common use.

SCHÜFFNER *et al.* (pp. 61, 908, 909) have made further studies on retrofection in *Enterobius* infection, and claim that in clean adult persons chronic enterobiasis is the result of this process, not of eggs conveyed on fingers or by dust. The anus should be washed frequently to ensure removal of all eggs before hatching—if this is done effectively every 6 hours, with strict attention to night-time, the worms may be eliminated, but this is rarely possible. Washing every 8 hours can markedly influence the infection, and under this régime the degree of infection suddenly decreased in one case on the 6th day, and only stragglers remained afterwards. These papers contain considerable detail on the longevity of female worms and the development of larvae in the eggs.

SANDOSHAM (p. 387) has found *E. vermicularis* in three Primates in the London Zoological Gardens, namely a chimpanzee, a gibbon and a marmoset. He discusses the public health significance of these findings.

TORRICO (p. 826) found high rates of infection in children in Bolivia, rather higher in boys than in girls.

The relationship between *Enterobius* infection and appendicitis is discussed by ROCKENSCHAUB (p. 184), and by BLÜMLEIN (p. 667) who found it in 75 per cent. of 81 cadavers in Germany, chiefly in the appendix. WELCKER (p. 909) concludes that toxins from the worms can cause pseudo-appendicitis, or even lymphadenitis of the glands in the meso-appendix; true appendicitis can be caused by entry of the worms into the wall of the appendix. He (p. 911) describes somewhat similar conditions probably due to *Ascaris*. SYMMERS (p. 748) thinks that the evidence that *Enterobius* can cause appendicitis is by no means conclusive. The worm sometimes gains access to the peritoneal cavity and is treated as a foreign body, and the author quotes 3 cases in which invasion of parenteral tissues was proved.

ERNST (p. 185) has used with success tablets of Contraverm (containing phenothiazine and phenolphthalein) in the treatment of *Enterobius* infection. He

claims that it is cheap, non-toxic, easy to take, necessary on one day only, and will kill young and old worms. KEIZER (p. 578) reports two cases of acute anaemia after treatment with phenothiazine during several days. He thinks that it should be given for one day only in a dosage of 120–150 mgm. per kgm. of body weight, provided that there are no signs of anaemia, hepatitis or nephritis.

KLOSA (p. 62) writes favourably of benzene hexachloride (BHC) in *Enterobius* infection, in daily doses of 10–20 mgm. for children, on 3 successive days, repeated if necessary, after an interval of 4–5 days. BREDE (p. 491) has used BHC with a good deal of success, though he was not able to eradicate the worms from all the patients. He advocates cold sitz baths and finger-nail hygiene as well as drug treatment. Details will be found in the original abstract. LENDLE and SCHNEIDER (p. 912) have studied the toxicity to man of single and repeated doses of BHC. Repeated doses have a cumulative effect.

ZIMA *et al.* (p. 186) refer to the composition of Egressin, a derivative of carbaminic acid, for the treatment of *Enterobius* infection. EICHHOLTZ and HOTOVY (p. 187) found it to be well tolerated by volunteers and useful in various infections of animals. SAUER and WEISSFLUG (p. 188) used it with success in a number of patients, though some 10 per cent. were not benefited. For dosage the original abstract should be consulted.

SIUNG (p. 279) treated *Enterobius* infection by giving benadryl daily for several days, with modest success.

*Trichuris*.—BURROWS (p. 61) calculates that in *Trichuris* infection the average number of ova per gramme of faeces is between 200 and 300 per female worm.

The commonest helminthic infection of the appendix found by SÁNCHEZ CASTELLANOS (p. 185) was with *Trichuris*.

BASNUEVO *et al.* (p. 1137) have used hexylresorcinol as an enema reaching the caecum, for the treatment of *Trichuris* infection. If this fails the drug may be given by duodenal sound, alone or with tetrachlorethylene.

*Trichinella, etc.*—TRUB and GAASE (p. 913) report two outbreaks of *Trichinella* infection in Germany, from pork and sausage meat. They stress the point that positive findings in meat inspection depend too much on chance, and that other methods, such as digestion or serological tests in pigs, should be added. Results in serological tests depend on the quality of the antigen used, and more than one may be needed.

ROTH (p. 1034) shows that in Norway foxes and mink are heavily infected with *Trichinella*, and in Greenland dogs and white bears.

ALICATA and RICCI (p. 1033) report on outbreaks of trichiniasis in Italy and Sicily; it is uncertain how these originated.

Writing of trichiniasis in Canada, STANYON (p. 914) warns of the danger of eating improperly cooked pork or pork products, but HARRINGTON *et al.* (p. 280) show that the processing of pork according to U.S. Federal meat inspection regulations is effective against this infection.

RAPPAPORT and WELLS (p. 1034) report studies on the immunity in mice given a single light infection of *Trichinella*.

AIKAWA *et al.* (p. 915) have studied the relationship of blood and extracellular fluid to *Trichinella*, in relation to the oedema which occurs.

MINNING and DING (p. 1035) gave hetrazan to mice 24 hours after infection with *Trichinella*, and found that it had some effect in reducing the subsequent intestinal infection. RIEDEL (p. 388) shows that sulphanilamide and sulphamerazine had some beneficial effect in experimental trichiniasis, but Fouadin was not found useful by SUREWICZ (p. 388).

An authentic case of human infection with *Capillaria hepatica* is reported by McQUOWN (p. 183).



CRUSZ and SIVALINGHAM (p. 667) report *Gongylonema pulchrum*, a parasite of ruminants, in a man in Ceylon, and GAUD and CHABAUD (p. 667) in a woman in Morocco.

Charles Wilcocks

## MALARIA

MOISE, R. Il problema della malaria in Somalia e l'impostazione di una campagna di lotta. (Relazione preliminare.) [**The Problem of Malaria in Italian Somaliland and Plans for Control**] *Riv. di Malariologia*. 1951, Oct.-Dec., v. 30, Nos. 5/6, 229-56, 17 figs. & 3 maps. [18 refs.] English summary.

This survey of malaria in Italian Somaliland is based on extensive personal observations and a study of published reports, but is, of necessity, very incomplete. The intensity of malaria infection varies greatly in different parts of the country and from year to year, but for the country as a whole there is no other disease of comparable public health importance. There is a close relationship between anophelism and the degree of immunity of the indigenous population. In parts of the country epidemics of malaria are not uncommon.

No census of the population has ever been made: it is estimated to be about 1,200,000. The people are of mixed race. The chief centres of population are found along the coast and along the courses of the Uebi and Giuba Rivers. Spleen and parasite indices in many of these places are indicated on maps.

The predominant malaria vector is *Anopheles gambiae*, by far the most prevalent species; its larvae are found in the usual great variety of breeding places. *A. funestus* is widespread but much less frequent. *A. pharoensis* and *A. coustani* are found here and there along the lower reaches of the Uebi Scebeli. *A. squamosus* and *A. nili* have been found in the neighbourhood of the village Duca degli Abruzzi.

*Plasmodium falciparum* is the predominant parasite: *P. vivax* is frequently found in young infants. *P. ovale* has been frequently reported. Blackwater fever is rare.

Malaria control measures are attended with special difficulties, the chief of which are due to nomadism, great distances, the low economic and social level, and very poor means of communication. Antilarval measures have a very limited field of applicability. Residual insecticidal sprays promise most hope of success in selected areas. The author formulates a scheme whereby work might be started along this line.

Norman White

MARA, M. Relazione sulla attività svolta dalla sede in Eritrea negli anni 1950-1951. [**Malariological Observations in Eritrea in 1950-51**] *Riv. di Malariologia*. 1951, Oct.-Dec., v. 30, Nos. 5/6, 277-85. English summary (9 lines).

The English summary appended to the paper is as follows:—

"The author, who is a malariologist of the Institute 'E. Marchiafava', relates the malariological observations made in Eritrea during the years 1950-1951. During this time examination of 22,000 mosquitoes was carried out and a classification of the different species, of which 16% *Anophelines*, 77% *Culicidae* and 7% *Aedes* was made. Experiments were also made on the toxicity of insecticides and the behaviour of *A. gambiae* towards DDT.

"Further research is still going on on the ecology and distribution of *Culicidae* in the Eritrean Territory, on the epidemiology of malaria and on effective control of adult mosquitoes."

See also p. 913, EAST AFRICA HIGH COMMISSION, **East African Malaria Unit Annual Report 1951.**

BLUMBERG, B., MCGIFF, J. & GUICHERIT, I. **Malaria Survey among the Bush Negroes of Marowynne District, Surinam, S. A., in 1950.** *Documenta Med. Geograph. et Trop.* Amsterdam. 1952, Mar., v. 4, No. 1, 2-4.

Spleen and parasite rates were taken in two groups of "Bush Negroes" living near the mines of the Surinam Bauxite Company. Among those in close proximity to the mines they were respectively 3.7 and 12 per cent.; in the more distant group they were 33 and 18 per cent. The endemicity indices (percentage of those showing either parasites or spleen) were 15 and 42 per cent. *Plasmodium falciparum* was the commonest parasite in both areas. The difference between the two groups may be due to frequent treatment of fever in those living near the mines.

G. Macdonald

HALL, W. H. & LOOMIS, G. W. **Vivax Malaria in Veterans of the Korean War. A Preliminary Report of 25 Cases.** *New England J. of Med.* 1952, Jan. 17, v. 246, No. 3, 90-93.

In 1945 and 1946 *P. vivax* malaria was a common disease among patients in the Minneapolis Veterans Hospital, most of whom had seen service in the south-west Pacific. Between September 1948 and May 1951 no case was seen. Between May 30 and July 21 1951, 25 patients with *P. vivax* malaria were admitted: these patients had all acquired the infection in Korea. The average length of stay in Korea was 8.5 months. Suppressive medication, chloroquine once a week, had been taken regularly by only 11 of the patients. Sixteen of the patients were admitted to hospital in Minneapolis during the primary attack of malarial fever: 8 patients had had one previous attack of malaria and one patient had had 2 attacks. Only 5 patients had had chills and fever suggestive of malaria while in Korea. One patient who took no suppressive drug had his first malaria attack one year after leaving Korea. Alternate cases were treated with chloroquine or pentaquine and quinine; chloroquine suppressed fever and parasitaemia rather more quickly than did quinine and pentaquine.

Norman White

LACHMAJEROWA, J. [LACHMAJER, J.] **Wintering Conditions of Females of *Anopheles maculipennis atroparvus*.** *Bull. State Inst. Marine & Trop. Med., Gdansk, Poland.* 1952, v. 4, No. 1, 95-6. [Also fuller version in Polish 79-93, 3 charts & 1 fig. (12 refs.) & in Russian 93-5.]

The author of this paper has studied the habits of *Anopheles maculipennis atroparvus* in winter quarters at different temperatures. In the vicinity of Gdansk [Danzig], females of this species have contact with human beings during the winter, but their settlement near human beings does not have a mass character. The number of females in the winter quarters varied with the temperature. When the temperature dropped below 5°C., only a few specimens were found, in the most sheltered spots. The air humidity in the winter quarters did not drop below, on the average, 70 per cent. Below 5°C., none of the females was found freshly fed. The ovarian follicles and ampullae increased slowly in size during the winter, but, owing to the death of the older females, the modal size of the ampullae was greater in January than in February.



Most of the winter quarters did not favour the development of the malaria parasite in the mosquito, and the author concludes that the greatest danger of malaria transmission is in the month of July.

A. J. P. Goodchild

ROZEBOOM, L. E. **The Significance of *Anopheles* Species Complexes in Problems of Disease Transmission and Control.** *J. Econom. Entom.* 1952, Apr., v. 45, No. 2, 222-6, 1 fig. [10 refs.]

Phenomenal success has been achieved in malaria control by the application of residual sprays of DDT to the insides of houses. This is because the most important vector species of *Anopheles* are highly domestic, entering houses to feed and to rest after feeding. There are, however, exceptions, such as *A. bellator* in Trinidad, which feeds out of doors, and *A. minimus flaviviridis* in the Philippines, which rests only briefly or not at all within the house.

The author of this paper considers these facts in relation to the possible evolution, as a result of intensive use of residual insecticides, of strains of *Anopheles* having different behaviour characteristics. The segregation of species as a consequence of geographical isolation is discussed with reference to the *A. maculipennis* complex of the Palaearctic region. Some of the physiological differences between the species of this complex are mentioned, and experiments on cross fertilization are described. Although cross fertilization occurs readily, there is a high larval mortality among the hybrids, and, when offered a choice of females, the males do in fact show a marked preference for their own species. Within these geographically separated species, differences of behaviour and physiology may be observed in sub-species and in local populations. The author has seen this in the *A. punctulatus* group in the Australasian region. *Anopheles pseudopunctipennis*, and also *A. bellator*, vary in their tendency to enter houses, in different parts of their range. Since variations of this sort are to be found in nearly all anopheline mosquitoes, it seems possible that, just as domesticity and habitual feeding on man are probably modifications of the originally wild habit, so the widespread use of residual insecticides may favour the selection of outdoor feeding and resting strains of *Anopheles*, and the site of transmission of malaria and other diseases may be transferred from indoors to outdoors.

A. J. P. Goodchild

LÜDICKE, M. & PIEKARSKI, G. Über die Gametenbildung von *Plasmodium falciparum* (Welch 1897). [**Gamete-Formation in *Plasmodium falciparum***] *Zent. f. Bakt.* I. Abt. Orig. 1952, Jan. 31, v. 157, No. 7, 522-39, 15 text figs. & 6 figs. on 2 pls. [27 refs.]

The authors describe the nuclear processes taking place in the course of gamete-formation and fertilization of *Plasmodium falciparum*, for the study of which they used blood-films from patients showing numerous crescents and the intestinal contents of *Anopheles maculipennis* taken at various intervals after the mosquitoes had fed on these patients. The preparations were examined fresh and after staining by Giemsa's method.

In the microgametocytes the nucleus first assumes the appearance of a dense scattered chromatin network containing about 6 sets of paired (diploid) chromosomes. These eventually give rise, by endomitotic division, to up to 6 nuclei of the microgametes, each with a haploid set of chromosomes, while the "flagellar" parts of the microgametes can already be recognized within the cytoplasm of the gametocyte before they bud off from its surface. After detachment of the gametes there is sometimes left behind a nuclear residue, which, in the authors' opinion, does not correspond to a reduction-body. The macrogametocytes undergo similar changes, producing 3-4 sets of chromosomes. The authors confirm the existence of a maturation process, manifested by the extrusion

of a reduction-body containing Feulgen-positive chromatin. Fertilization is initiated by the attachment of a microgamete to a macrogamete, with which it is connected by means of a cytoplasmic "bridge" adhering to the point where its nucleus is situated. After fertilization, the zygote nucleus undergoes mitotic divisions, in the course of which the nuclear material gives rise to 30-60 daughter-nuclei. The subsequent development of the zygote has not been studied.

The nuclear changes described are clearly illustrated by a number of figures and photomicrographs.

C. A. Hoare

JEFFERY, G. M. **Observations on a Gametocyteless Strain of *Plasmodium falciparum*.** *J. National Malaria Soc.* 1951, Dec., v. 10, No. 4, 337-44, 1 fig.

A description is given of a strain of *Plasmodium falciparum* which ceased to produce gametocytes after a number of direct passages from man to man. After the strain had been transmitted to a patient by mosquitoes, it was passaged directly through 7 others, in which gametocytes were still present. However, in 19 subsequent blood-passages through 24 patients, the strain ceased to produce gametocytes. Though a few were seen in two blood films (8th and 13th passages), none was found during the last 14 passages. Moreover, no infection was ever produced in 1,865 mosquitoes (*Anopheles quadrimaculatus*), batches of which were allowed to feed on these patients on 52 separate occasions. It is noted that the type of parasitaemia and clinical course of the infection with this strain were similar before and after loss of gametocytes.

C. A. Hoare

See also p. 910, LOEHNING & VAN BAAREN, **A Simple Method for Staining Trypanosomes and Plasmodia of Malaria in Tissue Sections.**

KRÜPE, M. Malariaplasmodien im "agglutinierten Dicken Tropfen"-Präparat. [**Malaria Parasites in Agglutinated Thick Blood Films**] *Ztschr. f. Tropenmed. u. Parasit.* Stuttgart. 1952, Feb., v. 3, No. 3, 412-14.

A description is given of a new modification of the thick blood film for the detection of malaria parasites. A drop of the patient's blood is mixed on a slide with rabbit serum containing agglutinins for human erythrocytes. The resulting thick film is stained in the usual way by Giemsa's method. In this preparation the red cells are not completely haemolysed and retain their regular outline, while the parasites are less shrunken than in the conventional thick film and can be readily identified. As regards the platelets and leucocytes, they are usually separated from the erythrocytes and cannot be mistaken for parasites.

C. A. Hoare

RAFFAELE, G. Dati nosografici sull'infezione sperimentale da "*Plasmodium falciparum*". [**Pathological Data Concerning Experimental Infection with *Plasmodium falciparum***] *Riv. di Malariologia.* 1951, Oct.-Dec., v. 30, Nos. 5/6, 217-27. English summary.

Among patients to be treated with malariotherapy there are not a few in whom *P. vivax* infections fail to produce the minimum number of febrile attacks necessary to obtain good results. In such cases the Ettore Marchiafava Institute has recourse to *P. falciparum* infections. This paper reports the experience gained during the treatment of 60 such cases. Thirty-eight patients were infected with sporozoites, 22 were inoculated with infected blood.



"Pernicious" symptoms developed during the course of the infection in 18 of the 22 patients inoculated with infected blood, and in 16 of the 38 infected with sporozoites. The infections were controlled with quinine. The immunity that developed gave a high degree of tolerance towards parasites in the peripheral blood. Fifteen months after recovery from the primary attack of malaria reinoculation with the same strain of parasite produced similar symptoms to those of the primary infection but the infection was much more easily suppressed with quinine than was the primary infection.

Nine cases of haemoglobinuria occurred among a group of 30 patients infected with the same strain of *P. falciparum*. This strain emanated from a district of Italy in which no case of haemoglobinuria had recently occurred. All 9 patients had had numerous recrudescences and had been repeatedly treated with quinine.

There was no correlation between the amount of infected blood inoculated and the severity of the malaria attack.

The average length of infection was 5 months 21 days: in a third of the patients it was more than 6 months.

Norman White

SHIBATA, S. **On some Overlooked Aspects of Malarial Relapse, with special reference to its Wavy, Regular and Periodical Outbreak after the Subsidence of Former Attack.** Reprinted from *Acta Path. Japonica*. 1951, v. 1, No. 3, 145-55, 3 figs. [21 refs.]

If primary attacks, recrudescences, relapses and recurrences of malaria are all grouped under the one heading of "attacks", the frequency of multiple attacks is found to correspond to a constant relapse rate, so that the chance of a person who has had 5 attacks having a sixth is the same as that of a person who has had one having a second. Study of the time interval between attacks shows an irregular distribution which can be analysed and corresponds to a periodicity in the probability of attacks subsequent to the first, rather than a constant liability.

Recrudescence and relapse, as defined by JAMES, have a similar periodicity; recurrences have a longer periodicity, which is, however, seen only in *Plasmodium vivax* malaria of temperate and subtropical climates, not in that of tropical climates or in any *P. falciparum* infections. The delayed primary attacks of *P. vivax* malaria in Europe correspond to the periodicity of recrudescences or relapses, suggesting that the phenomenon is essentially a simple suppression of the primary attack.

The paper is illustrated by mathematical examples giving the constants for the Poissonian curves for a number of series.

G. Macdonald

TORRES ESTRADA, A. **Manifestaciones oculares del paludismo. [Ophthalmic Manifestations in Malaria]** *Gac. Méd. de México*. 1951, Mar. 31, v. 81, No. 1, 30-48, 2 maps.

As long ago as 1940 the author read a communication on supra-orbital neuralgia occurring in malaria; in 1949 the present paper was read, covering much the same ground but amplifying the former. It concerns 300 patients, 217 females and 83 males. The females would appear to be much more susceptible to this neuralgia than the males. In a table are given the following details of each of these patients: age, sex, history of previous malaria, immunity or not to malaria [no clear indication is given as to the meaning of this], whether they had been born or had lived in a malarious district, place of residence, existence of supra-orbital and occipital neuralgia, other complications and

previous diagnoses. The forms of malaria were masked (*malaria larvada*) in that parasites were not found and Henry's reaction was positive in only a few. The neuralgia might be very severe and operation for sinusitis might be undertaken without relief, and even mental disturbance might occur. In 47 of the patients other manifestations were present, notably papillitis in 7, glossopharyngeal neuritis with dysphagia (7), keratitis (11), paralysis of the extrinsic eye muscles (4), facial palsy (1).

Treatment by anti-malaria drugs, quinine or proguanil, was usually successful. In brief, supra-orbital neuralgia, in absence of sinusitis or other obvious cause, should make one think of "masked malaria". H. Harold Scott

MURGATROYD, F. **The Chemotherapy of Malaria.** *Postgraduate Med. J.* 1952, Jan., v. 28, No. 315, 5-10.

An account of current knowledge and practice, by the late Professor of Clinical Tropical Medicine in the London School of Hygiene and Tropical Medicine [University of London].

MOHR, W. Resochin-Therapie der Malaria. [**Resochin Treatment of Malaria**] Reprinted from *Verh. Deut. Ges. inn. Med.* München. 57. Kongress 1951, 264-8, 2 figs.

The author regards Resochin (which he is at pains to point out is essentially the same as Aralen, Chloroquine, Tanakin and Nivaquine) as the best and quickest-acting modern anti-malarial. It is effective in *P. vivax*, *P. malariae* and medium-severe *P. falciparum* infections. In severe (comatose) *P. falciparum* cases he advises parenteral atebirin [mepacrine]. He recommends as routine treatment 0.75 gm. Resochin immediately, 0.75 gm. 6 hours later; 0.5 gm. 12 hours after the first dose, and finally 0.5 gm. 12 hours later. The total dosage is 2.5 gm., given in 24 hours.

Resochin has no appreciable action on *P. falciparum* gametocytes or EE forms of *P. vivax*. A 3-day course of plasmoquine following the Resochin (0.01 gm. twice daily) is advised.

The author states that Resochin is as effective as atebirin in giardiasis. It is successful also in amoebic hepatitis and hepatic abscess, but not in amoebic gut infections. In dealing with amoebiasis the dose required is greater and the course of treatment longer. B. G. Maegraith

FOY, H. & KONDI, Athena. **Effect of Daraprim on the Gametocytes of *Plasmodium falciparum*.** [Correspondence.] *Trans. Roy. Soc. Trop. Med. & Hyg.* 1952, May, v. 46, No. 3, 370.

The schizonticidal effect of Daraprim is now well established [this *Bulletin*, 1952, v. 49, 11, 663-666, 751]. The present authors, in Nairobi, have demonstrated its efficacy in rendering gametocytes of *P. falciparum* uninfected to *Anopheles gambiae*.

In an African with *P. falciparum* malaria and parasitaemia, 2 crescents were found per 44 leucocytes: the sex ratio of the gametocytes was about 1:1 then and throughout the experiment. The patient was exposed to bites on the arm by 30 to 40 uninfected *A. gambiae*. Five mosquitoes which had fed were incubated at 26° to 29°C. for 18 days, when sporozoites were found in their salivary glands.

Immediately after this feeding, the patient received 20 mgm. Daraprim and batches of mosquitoes were fed on him again at approximately 2-day intervals on 6 occasions. After 18 days' incubation, all the mosquitoes fed after Daraprim were negative for sporozoites, though many gametocytes were present from the



fifth day onwards. On the 2nd and 3rd day after these batches had been fed, additional doses of Daraprim (50 mgm. each) were given, but clinical and blood features suggested that these two doses were not necessary.

The details of the experiment are shown in a table, which indicates that after the 5th day from the first administration of Daraprim, the blood of the patient contained 11 per cent. of crescents, rising to 50 per cent. on the 8th day, while rings were absent, the temperature was normal and the glands of the mosquitoes were negative throughout this period.

H. J. O'D. Burke-Gaffney

MENDOZA, J. B. **Trial with *Clostridium tetani* Toxoid in the Inhibition of Malaria Relapse.** *J. Philippine Med. Ass.* 1952, Feb., v. 28, No. 2, 61-6.

In 1948 GARCIA reported remarkable success in the prevention of malaria relapses by the subcutaneous injection of tetanus toxoid following the course of anti-malarial treatment [this *Bulletin*, 1949, v. 46, 1112]. The author of this paper describes his attempts to confirm Garcia's findings. He had under observation for one year 115 patients with *P. vivax* and 29 with *P. falciparum* infections. These were all in Manila, a non-endemic area: the patients had been infected elsewhere in the Philippines. They were treated with either mepacrine or aralen. Approximately half of the patients received an injection of 1 ml. tetanus toxoid one week after the clinical cure and a second similar injection 3 weeks later. There was no significant difference in the relapse rate of the two groups of patients. In other words tetanus toxoid failed to exercise any anti-relapse activity in these patients.

Norman White

LIPPARONI, E. **Possibilità e limiti della lotta antimalarica in Somalia. [Possibilities and Limitations of Anti-Malarial Control Work In Italian Somaliland]** *Riv. di Malariologia.* 1951, Oct.-Dec., v. 30, Nos. 5/6, 257-75. English summary.

The author describes the geography, geology and climate of Italian Somaliland, a territory covering 500,000 square kilometres with 1,250,000 inhabitants. Special attention is paid to conditions which determine the marked differences in anopheline prevalence which characterize different areas and the consequent differences in types of malaria endemicity to which they give rise. Any local scheme for the control of anophelines calls for persistent effort. Suppressive medication with chloroquine or camoquin would be of value. A noteworthy reduction in the incidence of malaria might be possible by such means, but eradication of the disease at the present time is not a practicable proposition.

Norman White

NASIR-UD-DIN, M. **A Year's Work of the National Malaria Control Teams in East Pakistan (1950).** *Pakistan J. of Health.* 1952, Jan., v. 1, No. 4, 21-41, 8 figs. [10 refs.]

A WHO Malaria Control Demonstration Team worked in East Pakistan in 1949 and 1950, and its presence led to the formation of two national teams, assisted by UNICEF, the activities of which over one season are recorded. They worked in Parashuram, where the vector is *Anopheles minimus* and population protected is 61,000, and in Gabtali where the vector is *A. philippinensis* and the population concerned 23,000. One round of spraying was completed, with DDT wettable powder in houses and animal shelters, the mean dose of DDT applied being 187 mgm. per sq. ft. in the first area and 106 in the second.

The work done is tabulated with details of staff and costs, which worked out at As [annas] 8 and As 6 (roughly 13 and 10 pence) per person protected. Details of spleen rates, parasite rates and infant parasite rates before and after spraying are recorded from both sprayed and unsprayed areas; there were significant reductions in all in the sprayed areas and seasonal increases in the others. Vector anophelines disappeared entirely from treated places, and tests showed that the treated walls remained lethal to them for at least 13 months in the first area and 9 months in the second. On this evidence it is decided that one annual round of treatment will be sufficient to break the cycle of transmission in both areas although it normally continues for more than half the year.

[The account of one season's work is quite convincing, but the reviewer cannot agree with the validity of the evidence that one annual round will be sufficient.]

G. Macdonald

GILROY, A. B. **Field Trials of D.D.T. and B.H.C. in Assam.** *Indian J. Malariology*. 1951, June, v. 5, No. 2, 171-82.

Comparative trials were made of suspensions of DDT and BHC in a part of Assam where *Anopheles minimus* is the vector of malaria; *A. vagus* and *A. leucosphyrus* also occur. The houses used were plastered with a mud-cowdung mixture, and had thatch roofs and no ceilings. Two houses were kept as controls; 5 were treated with DDT at doses of 45, 90, 135, 180 and 225 mgm. per sq. ft., and 2 with BHC at doses of 10 and 20 mgm. of the gamma isomer per sq. ft. All were fitted with window traps, and at appropriate times counts were made of dead anophelines on sheets spread on the floors.

There was a significantly higher proportion of unfed mosquitoes in the traps of untreated houses than in the treated houses, and their mortality was high (82 per cent. in 24 hours) even in those which had not been treated. An irritant effect of all doses of DDT and the low dose of BHC was demonstrated by the high proportion of the total catch which occurred in window traps. [The evidence might equally show that the high dose of BHC killed mosquitoes before they could reach the trap, none being irritated.]

The total 24-hour mortality is given for periods of 5, 8 and 12 weeks, for all treatments, and in weekly detail up to 7 weeks for 45 mgm. DDT and 10 mgm. gamma BHC.

The most effective treatment was 20 mgm. gamma BHC, which gave a mortality of 98 per cent. at 12 weeks and 97 per cent. at 15 weeks. The most effective dose of DDT was 135 mgm., which gave an 85 per cent. mortality over 12 weeks, both smaller and larger doses being less effective. The relative inefficiency of larger doses was obvious at 5, 8 and 12 weeks, though it cannot be explained.

It is concluded that where local conditions such as the frequency of re-plastering makes a 6-week cycle desirable, 10 mgm. gamma BHC and 45 mgm. DDT are equally suitable. Where a longer cycle is desirable 20 mgm. gamma BHC is preferable to any DDT dosage.

G. Macdonald

MERCADO, Teresa I. & COATNEY, G. R. **The Course of the Blood-Induced *Plasmodium berghei* Infection in White Rats.** *J. National Malaria Soc.* 1951, Dec., v. 10, No. 4, 359-65, 2 figs. [12 refs.]

The authors describe observations on the course of blood-induced infection with *Plasmodium berghei* in young white rats (6 weeks), each inoculated intravenously with about 5,000 parasitized erythrocytes.

The infection in rats was of 2 types: one lethal, the other leading to recovery. In lethal infections there was a prepatent (incubation) period of 2-5 (average



3.3) days, while the patent period lasted 8 to 21 (average 12.2) days, with parasitaemia reaching the peak at 10 to 15 (average 11.5) days, and death ensuing usually 24 hours later; the average number of merozoites produced by each schizont was from 5.5 on the 1st patent day to 14.1 on the 8th; by the 16th day their number fell to 5.17, rising again to 12.2 on the 18th. In recovered infections the incubation period was similar, but the patent period lasted from 16 to 22 (average 18.6) days, and the peak of parasitaemia occurred at 7 to 16 (average 11) days; the mean number of merozoites per segmenter was from 3 to 8 on the 2nd and 3rd days respectively, reaching 16 on the 5th day, after which their number gradually fell to 4.6 on the 16th day, rising again to 9.5 on the 19th day.

In order to ascertain the degree of anaemia produced in the course of the infection, daily red cell counts were made. In the lethal infections the count dropped from 5.32 million per cmm. (normal) to 0.78 million, after which they rose to 3.28 million on the 18th day. The infected animals showed a progressive yellow discoloration of the skin; the eyes became yellowish white, and there was general loss of condition. In the terminal stages of the disease, these symptoms were intensified, and shortly before death were accompanied by laboured breathing and somnolence. The surviving animals soon recovered their normal condition.

C. A. Hoare

ODDO, F. G. & BRUNO-SMIRAGLIA, C. La persistenza dell'infezione da *P. gallinaceum*. Pigmento melanico, parassiti endo- ed esoeitrocitici. [Persistence of *P. gallinaceum* Infection. The Pigment, and Endo- and Exo-Erythrocytic Parasites] *Riv. di Parassit.* Rome. 1951, Oct., v. 12, No. 4, 215-26, 10 figs. [17 refs.] English summary.

The authors describe the course of infection of fowls with *Plasmodium gallinaceum*, with special reference to the appearance and changes in the pigment at different stages of the disease, the parasitological findings, and the histopathology of the spleen, liver and brain. The material for this study comprised blood and tissue smears, as well as sections of organs, taken from birds which were killed or had died at different intervals from the time of inoculation.

During the acute phase of the infection—between the 1st and 18th days of parasitaemia—the organs contained “young” pigment of recent formation, represented by minute granules, while erythrocytic parasites were constantly found in the tissue smears, and EE forms appeared in the brain after a fortnight. In birds examined between 1 and 5 months after termination of the acute phase, the amount of pigment in the organs gradually decreased with time, and was represented chiefly by compact masses which had lost their granular character. In addition to this “old” pigment, deposited at an earlier stage of the infection, the tissues contained minute granules of recently-formed pigment, similar to that found in the acute stage of the infection. This provided evidence of the persistence of the erythrocytic infection, which was confirmed by the finding of rare parasites in smears of the spleen tissue. In a 3rd group of birds, examined between the 3rd and 7th months after termination of the acute phase, agglomerations of “old” pigment were still present, but their amount decreased with time, until it became very scanty. At this period, no parasites could be detected in any of the organs.

From these observations it is concluded that latent infection and relapses in fowl malaria can be accounted for by the persistence in the internal organs of the erythrocytic cycle alone.

C. A. Hoare

TERZIAN, L. A., STAHLER, N. & WARD, P. A. **The Effect of Antibiotics and Metabolites on the Immunity of Mosquitoes to Malarial Infection.** *J. Infect. Dis.* 1952, Mar.-Apr., v. 90, No. 2, 116-30, 5 figs.

Terzian has already shown that a particular concentration of sulphonamides increases the susceptibility of mosquitoes to infection by *Plasmodium* [this *Bulletin*, 1951, v. 48, 447]. In the present series of experiments, the mosquitoes are fed on sugar solutions (with or without added drug) till they are 72 hours old. A cage of those which have received the drug is then put on an infected chick (*P. gallinaceum*); it is essential to put a control group on the same chick at the same time. The result is measured by the number of oöcysts which develop: the median count is regarded as the most suitable single parameter: significance of difference is assessed by the chi squared test.

Taking the experiments on *Aedes aegypti* and sulphadiazine, it is clear that a 0.01 per cent. concentration in the sugar does not affect the number of oöcysts: concentrations of 0.05 and 0.10 per cent. lead to a higher number of oöcysts and in that sense favour the parasite: the effect disappears with 0.30 per cent. of the drug, which then has no measured effect either way.

In a similar way the authors show that certain concentrations of para-aminobenzoic acid, aureomycin and streptomycin, in the sugar meals, increase the number of oöcysts which subsequently develop. Folic acid has a contrary effect. When, however, the work is repeated with *Anopheles maculipennis*, contradictory results are obtained: in this case the effect of para-aminobenzoic and folic acids is as before, but sulphadiazine or aureomycin reverse these effects, and reduce the number of oöcysts.

The results are not yet explained; it is of interest to observe that these substances have effects (either positive or negative) on the establishment of infections of a protozoon in an insect.

P. A. Buxton

HANSON, R. O. & TATUM, A. L. **Drug, Host and Parasite Interrelationships in the Treatment of Avian Malaria (*Plasmodium cathemerium* in Canaries).** *J. Infect. Dis.* 1952, Mar.-Apr., v. 90, No. 2, 105-9.

As in *P. vivax* infections of man, a state of latency is a marked feature of infection with *P. cathemerium* in canaries, and regardless of the method of injection, eradication of the parasites is accomplished only, if at all, by doses of drug which are not well tolerated. In an attempt to determine how infection with *P. cathemerium* becomes established in canaries the birds were injected with different numbers of parasites and pentaquine in maximum tolerated doses was given at various intervals after inoculation. Subinoculations were then made with the blood of the treated bird into fresh hosts and the presence or absence of infection in the latter was then determined. It was found that if the parasites were injected intravenously and treatment was withheld for 4 hours the resulting infection was refractory to treatment. When the numbers of *P. cathemerium* in the inoculum were small and simultaneous treatment with drug was given, subinoculation of the blood of the donor bird into a fresh host did not give rise to infection; if the number of parasites used was much larger infection did result in spite of treatment. These facts were taken to indicate that some defensive mechanism in the donor bird was incapable of rendering the larger number of parasites non-infective. Infection by blood from a latently infected host could be prevented in a fresh host by simultaneous administration of drug intravenously, whereas the same treatment failed to cure the donor bird. The conclusion was drawn that in the latently infected bird some parasites are inaccessible to the drug and continue to act as a source of the bloodstream forms.

J. D. Fulton



## BLACKWATER FEVER

MAEGRAITH, B. **Recent Advances in Tropical Medicine. No. 1. Blackwater Fever in West Africa.** *West African Med. J.* 1952, Jan.-Feb.-Mar., v. 1 (n.s.), No. 1, 4-10. [17 refs.]

This paper opens with a summary of the results of FINDLAY's investigations of blackwater fever in European and African military personnel in West Africa during 1941-45 [this *Bulletin*, 1950, v. 47, 329]. The author then reviews some of the factors which are believed to be concerned in haemolysis in blackwater fever. He found that normal tissue contains a lysin which is inhibited by substances in the blood plasma and that this inhibition is considerably reduced in sera from cases of actively-lysing blackwater fever. The importance of changes in plasma inhibitors has, however, still to be confirmed.

Irregular quinine suppressive or therapeutic dosage is a pathogenic factor of extreme importance in many cases of blackwater fever, but the disease may occur in those who have never taken quinine and exceptionally in persons taking other anti-malarial drugs. Immunity reactions resulting from *P. falciparum* infections may be important factors in the causation of haemolysis. Blackwater fever is likely to occur in those who have lost immunity or premunition to a particular strain of *P. falciparum* if they receive an additional infecting dose of the same strain.

About half the deaths from blackwater fever result from renal failure. The anuric patient usually dies but recovery may occur spontaneously. The author suggested that the whole condition was a vascular phenomenon; the cortex of the kidney becomes ischaemic to the extent of damaging the epithelium and shutting down the glomerular flow. The liver changes likewise seem to be dependent on vascular phenomena.

The treatment of blackwater fever is admirably summarized. Indications for the intravenous injection of plasma and salines are clearly described. Serious consequences, including fatal pulmonary oedema, may result from overloading with fluid, particularly in anuric cases. If the red cell count has fallen to 1.5 million per cmm. transfusion is necessary. It is absolutely necessary to check the donor's cells against the patient's plasma and *vice versa*. If malaria parasites are present in the peripheral blood a full therapeutic course of anti-malarial treatment is necessary: quinine and pamaquin should be avoided. For renal failure diuretics are useless. The administration of large quantities of alkali formerly used is of no value and may be harmful. *Norman White*

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 TRYPANOSOMIASIS

HENRARD, C. Répartition des glossines au Congo belge et au Ruanda-Urundi. [**Distribution of Glossinae in the Belgian Congo and Ruanda-Urundi**] *Inst. Roy. Colonial Belge Bull. des Séances.* 1951, v. 22, No. 4, 967-93. [95 refs.]

Collections of tsetse flies and published records have been examined with a view to showing on a map of the Belgian Congo the distribution of the various species of *Glossina*. In this paper the matter is briefly discussed but no map is given.

Fourteen of the known twenty-one species of *Glossina* occur in the Congo. *G. palpalis* is widespread except in the extreme south-east. Some differences in the distribution of the subspecies of *G. palpalis* (*palpalis*, *fuscipes* and

*martinii*) as given by ZUMPT [this *Bulletin*, 1941, v. 38, 74] and VANDERPLANK [*ibid.*, 1949, v. 46, 1013] are pointed out. *G. morsitans* subspecies *morsitans* occupies a large area in the south-east, of which the western limit appears to be about the Lomami and Lualaba rivers; the subspecies *submorsitans* occurs along the Garamba river in the north-east near the Anglo-Egyptian border. *G. pallidipes* exists in the same region as *G. m. morsitans* but extends northwards along the valleys between the lakes. *G. longipalpis*, a vector of animal trypanosomiasis, occurs mainly in the north-west along with *G. tabaniformis* and *G. fusca* though the latter is largely restricted to the eastwards of 24°E. longitude. *G. fuscipleuris* has been taken at various points along the eastern border, but *G. schwetzi* only about the mouths of the Congo and Kwango rivers. The East African species *G. brevipalpis* is found south of latitude 5°S.

The other species, *G. newsteadi*, *nigrofusca*, *haningtoni*, *severini* and *vanhoofi* occur only in small numbers and at places widely separated.

H. S. Leeson

See also p. 910, LOEHNING & VAN BAAREN, **A Simple Method for Staining Trypanosomes and Plasmodia of Malaria in Tissue Sections.**

JUSSIAINT & GASPARD. **The Trypanosomiasis. Sickness Difficult to disclose among the Goat.** *Bureau Permanent Inter africain de la Tsé-Tsé et de la Trypanosomiase. No. 185/T. Léopoldville (Congo Belge). [1952.]* 3 mimeographed pp.

KRANEVELD, F. C., HOUWINK, A. L. & KEIDEL, H. J. W. **Electron Microscopical Investigations on Trypanosomes. I. Some Preliminary Data regarding the Structure of *Trypanosoma evansi*.** Reprinted from *Proc. Roy. Netherlands Acad. Sci. Ser. C.* 1951, v. 54, No. 4, 393-9, 9 figs. on 2 folding pls. [17 refs.]

The authors record their electron microscope observations on the structure of the periplast and flagellum of *Trypanosoma evansi*. The blood of infected guineapigs was diluted with sodium citrate and Ringer's solution, and the trypanosomes were separated from the blood by centrifugation, after which they were suspended in saline, and finally washed in distilled water before drying. Though the water caused the trypanosomes to disintegrate, their structure could be more easily observed than in specimens fixed with osmic acid. The preparations were shadowed with gold and manganin, and micrographs were made with the electron microscope at 90 kV.

It was shown that the periplast of the trypanosomes contains from 60 to 80 longitudinal, almost parallel fibrils, about 40 mμ in width. They appear to be arranged in bundles, possibly corresponding to the so-called "myonemes" which have been described in trypanosomes seen under the light microscope. The flagellum consists of up to 9 cross-striated parallel fibrils enclosed in a cytoplasmic sheath. At its base the flagellum passes through a collar-like structure, which might be the point at which it issues out of the body.

The structures seen are clearly depicted in a number of figures.

C. A. Hoare

TOBIE, Eleanor J. **Loss of the Kinetoplast in a Strain of *Trypanosoma equiperdum*.** Reprinted from *Trans. Amer. Microscop. Soc.* 1951, July, v. 70, No. 3, 251-4, 2 figs. [10 refs.]

"The spontaneous loss of the characteristically permanent structure, the kinetoplast, has been reported in a strain of *Trypanosoma equiperdum* maintained in the laboratory in animals. This loss may have occurred gradually over a period of many years as indicated by the decreasing number of kinetoplasts per 1,000 trypanosomes since January, 1946. The fact that a few



trypanosomes with kinetoplasts can be found in akinetoplastic strains can explain the reappearance of the kinetoplast in these strains on the basis of multiplication of kinetoplastic individuals without assuming a genetic change."

AGOSIN, M., CHRISTEN, R., JARPA, A., ATIAS, V. A. & NEGhme, A. Cortisone y enfermedad de Chagas experimental. [**Cortisone and Experimental Chagas's Disease**] *Rev. Med. Chile*. 1952, Jan., v. 80, No. 1, 34-7. [31 refs.]

The following is a translation of the authors' summary :—

Oral and intramuscular administration of cortisone masks the symptoms of experimental Chagas's disease in mice, even though the infection is more intense than in the controls.

Pentaquine phosphate is incapable of counteracting the unfavourable effects of cortisone : on the other hand a combination of quinine sulphate and pentaquine phosphate brings about a reduction of parasitaemia and tissue parasitism, but does not prolong the survival time.

Cortisone alone or associated with the quinolines causes inhibition of the reticulo-endothelial system and absence of inflammatory response in treated animals.

Cortisone gives rise to a change in the tissue tropism of *T. cruzi*, which is accompanied by alterations of morphology in the leishmanial forms.

H. J. O'D. Burke-Gaffney

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## LEISHMANIASIS

ANSARI, N. & FAGUIH. Un nouveau milieu de culture pour *Leishmania*. [**New Culture Medium for Leishmania**] *Bull. Soc. Path. Exot.* 1952, v. 45, No. 1, 43-5.

After trials with various media, including N.N.N. to which different growth factors were added, the authors found that leishmanias grew readily and abundantly for over 3 weeks in placental juice and in placental broth, which are prepared as follows.

**Placental juice.**—The placenta, deprived of the cord, is finely chopped, pressed through linen cloth and filtered through cotton wool, after which the material is centrifuged at 3,000 revolutions for 30 minutes, forming 3 distinct layers. One volume of supernatant fluid, free of cells, is diluted with 5 volumes of saline, the fluid is passed through a Seitz filter under low pressure, and distributed in test-tubes in quantities of 5-7 cc.

**Placental broth.**—500 gm. of placenta are finely chopped, 1 litre distilled water is added to the material, after which the suspension is boiled for 30 minutes and pressed through linen cloth. It is then allowed to cool, filtered through moist Chardon paper, and 5 gm. salt are added to it. The fluid is finally autoclaved for 20 minutes at 120°C. and distributed in test-tubes.

C. A. Hoare

CHUNG, Huei-lan & FENG, Lan-chou, with assistance of Shui-lien FENG. **Observations concerning the Successful Transmission of Kala-Azar in North China by the Bites of Naturally Infected *Phlebotomus chinensis*.** *Peking Nat. Hist. Bull.* 1950-51, Dec.-Mar., v. 19, Pts. 2/3, 302-26. [33 refs.]

The data presented in this paper were collected from experimental work carried out in 1940 and 1941.

An experimental station was set up in the Western Hills outside Peking. *Leishmania*-infected dogs were kept in rooms to which wild sandflies had easy access. These rooms were closed in the early morning and sandflies were collected. The numbers of flies attracted by dogs during one night often amounted to hundreds and on one occasion 1,391 were collected. The percentage that had sucked blood was 98 and the average leishmania infection rate 71.1, 65.2 and 64.4 per cent. respectively, for the 3 dogs, and on rare occasions was 100 per cent. The sandflies were *Phlebotomus chinensis*.

Dissection of the flies showed an infection with leishmania of the proventriculus as early as the third and fourth days after feeding and of the pharynx and proboscis on the fifth day. When the infections were light, or there were no flagellates found, there was usually a heavy bacterial infection present: it is thought that this infection came from the secondarily-infected lesions from which these dogs suffered.

The mortality among the infected flies was very high; sometimes up to 90 per cent. died within 3 days and it was found necessary to devise methods of feeding them artificially in order to prolong their lives sufficiently for them to feed on a mammal for a second time. Raisins were at first used but it was found that fresh slices of ripe apples or pears were as good as raisins. These were placed on the bottom of the receptacle over which the glass lamp-chimney in which the sandflies were kept was placed.

Transmission experiments were carried out with hamsters. The animals were narcotized with urethane, the hairs on the abdomen were pulled out by hand and flies in test-tubes were applied to the denuded skin, not more than two in each tube. The flies usually fed or attempted to feed within 20 minutes; others made no attempt at feeding. Some of those that attempted to feed, on subsequent dissection showed the proventriculus "virtually choked" with flagellates; these the author considered to be "blocked flies". [This is surely a common finding; SMITH's "blocked" flies were "blocked" more anteriorly: this *Bulletin*, 1941, v. 38, 256.]

A total of 72 hamsters were subjected to bites by infected flies; of these 25 died and were not examined. (The experiment was interrupted in December, 1941 by the war.) Of the 47 surviving, 8, or 17 per cent., were found to be infected with leishmania.

The number of infected flies that were seen to feed or attempt to feed on the hamsters in the successful experiments varied from 7 to 68 and the number of these flies that actually sucked blood varied from 3 to 22. The interval between the infecting feed and the transmitting feed varied in different batches of flies from 3 to 15 days, but in no case where transmission occurred was the longest interval in at least one batch less than 6 days.

A few additional observations were made:

*P. chinensis* were found from the beginning of May until the end of September: there are indications that transmission may occur in nature from the end of May until at least the first week in September.

Three hamsters showed evidence of infection as early as 47, 63 and 64 days, respectively. The rest were kept for 5 to 9 months before being killed for examination.

The bacterial infection that the flies acquired from dogs with open sores prevents the development of leishmania infections in the flies and probably acts as a brake to transmission in nature.

However, the enormous number of flies that a dog can infect with leishmania in one night makes it probable that where infected dogs are found they are the main reservoirs of leishmania infection.

L. E. Napier



STONE, H. H., TOOL, C. D. & PUGSLEY, W. S. **Kala-Azar (Visceral Leishmaniasis) : Report of a Case with 34 Month Incubation Period and Positive Doan-Wright Test.** *Ann. Intern. Med.* 1952, Feb., v. 36, No. 2, Pt. 2, 686-93, 3 figs. [21 refs.]

- " 1. A case of kala-azar (visceral leishmaniasis) is presented.
- " 2. A minimal incubation period of 34 months is recorded.
- " 3. A positive Doan-Wright test for splenic neutropenia was obtained.
- " 4. Parallel bone marrow cultures were negative on regular NNN medium, positive on modified NNN containing defibrinated blood from the patient.
- " 5. Successful treatment with a single course of Neostibosan (3 gm.) was indicated by a fourth month follow-up period."

HENRY, A. J., MANSOUR, R., WATSON, A. G. & ZAKI, A. H. **Storage of Stilbamidine in the Animal Body.** [Correspondence.] *Nature.* 1952, May 17, 835-6.

Earlier work has suggested that stilbamidine (trans 4 : 4'-diamidinostilbene) is stored in the body for long periods after administration and may cause the late toxic symptoms experienced with this drug [this *Bulletin*, 1945, v. 42, 18, 783 ; 1948, v. 45, 775 ; 1949, v. 46, 1133]. Further experiments have now been carried out to determine the site of storage in order to explain the delayed toxic actions which occur in clinical practice. It has been found possible to extract stilbamidine from tissues by heating for some hours with 10 per cent. HCl on the water bath, and to estimate it by its fluorescence in solution or when spotted on filter paper. The drug is now stated to be absent from plasma at the end of a course of injections and likewise from red cells [previously HENRY and GRINDLEY (this *Bulletin*, 1943, v. 40, 122) had suggested that red cells acted as storage depots but experimentally FULTON and GOODWIN (*ibid.*, 1946, v. 43, 17) could not confirm this finding]. From experiments with sheep, rabbits and rats it is clear that the distribution in tissues varies widely in different animal species. In seeking further the explanation of the toxic results it is proposed to investigate the effect of storage of the drug on fat or mineral metabolism.

J. D. Fulton

SOONG, H. Y. & HO, E. A. **Determination of CD<sub>50S</sub> and Therapeutic Indices of Pentostam and Ureastibamine in Chinese Hamsters.** *Chinese Med. J.* Peking. 1952, Mar.-Apr., v. 70, Nos. 3/4, 140-43.

" In this experiment, the LD<sub>50</sub> of pentostam was found to be about the same in mice and Chinese hamsters, while that of ureastibamine showed wide discrepancy in the two kinds of animals. The LD<sub>50</sub> of ureastibamine in Chinese hamsters was 0.85 gm. per kilo body weight in comparison with 0.41 per kilo in mice. The toxicity of ureastibamine also varies widely in different samples. For example, the subcutaneous LD<sub>50</sub> of this drug was reported to be 2.0 gm per kilo in Chinese hamsters by Wang. The determination of the therapeutic index was based upon the toxicity data obtained in Chinese hamsters in this study.

" The therapeutic indices of pentostam and ureastibamine are about the same and the slight difference between the potency of these two drugs is not considered significant. Since pentostam has a constant composition and is very stable, it is a better drug to be used as a standard for the evaluation of other agents."

[See also this *Bulletin*, 1952, v. 49, 761.]

MALARD, A. Une petite épidémie de leishmaniose cutanée à Laghouat (Algérie). [A Small Outbreak of Cutaneous Leishmaniasis at Laghouat, Algeria] *Arch. Inst. Pasteur d'Algérie*. 1951, Sept., v. 29, No. 3, 219-21.

Oriental sore has been known to occur at Laghouat (Algeria) for a long time, but it is usually sporadic in its incidence; occasionally an epidemic occurs among newcomers and such a one occurring in the European military garrison during the last quarter of 1950 is reported.

During the period 21 patients with lesions clinically suggestive of oriental sore were seen; in 13 cases the lesion was on the lower limbs, in 5 on the upper, 1 in the lumbar region, 1 on the cheek and in 1 there were multiple lesions on the upper and lower limbs.

The typical lesion was round, about the size of a 5-franc piece, with sharply cut raised edges. In one place the ulcer showed hyperplasia and in other gangrenous necrosis. It was surrounded by reddish purple areola which was studded with small indurated prominences.

Leishmaniae were found in 7 cases and in the others the absence of bacteria and nature of the cells observed suggested that the clinical diagnosis was correct.

*Phlebotomus papatasi* is the transmitter of oriental sore in this area; other sandflies found are *P. minutus*, *P. parroti*, *P. perniciosus*, *P. fallax*, *P. sergenti* and *P. squamipleuris* var. *dreyfussi*. L. E. Napier

SIMONET, P. Remarques épidémiologiques sur six cas de bouton d'Orient observés à Beni Abbès (Sahara oranais) en 1951. [Epidemiological Note on Six Cases of Oriental Sore at Beni Abbès] *Arch. Inst. Pasteur d'Algérie*. 1951, Sept., v. 29, No. 3, 222-4.

In February 1951, 6 cases of oriental sore were observed at Beni Abbès in the Western Sahara, where a case was first reported by RAMES in 1939 [this *Bulletin*, 1940, v. 37, 351].

The population of the place consists of 1,155 Africans, 15 Europeans, and 2 Jews. The Europeans live in a military compound and in houses nearby, whereas the Africans live in separate quarters in a palm grove 300 to 400 metres away.

From January 20th to February 8th, 1951, the population was examined and 31 persons found presenting cutaneous lesions more or less suggestive of oriental sore. Smears were examined and in 6 cases *Leishmania tropica* was found.

These persons had apparently contracted the infection locally, as they had not been away from their homes for a long time.

In 3 cases the lesions were on the lower third of the lateral aspect of the leg and in 3 in the frontal region. Four of the patients were Arabs and in their cases the lesions were classical, but in the other two who were Negroes the ulcers were deep, the bases were smooth, and the edges scarcely raised.

Two of the patients were treated with anthiomaline, one by local and intravenous injections and the other by intravenous injections only: a cure was obtained in 20 days. The other 3 were each given 12 injections of glucantime and were cured in an average period of 17 days. The sixth patient was not treated but the ulcer healed spontaneously in about the same time.

The sandflies found in the locality were *Phlebotomus papatasi*, *P. parroti*, *P. fallax*, *P. minutus*, and *P. sergenti*. L. E. Napier



## FEVERS OF THE TYPHUS GROUP

CH'IN, K. Y., LIU, Wei-t'ung & LIU, Y. **Paralysis of Legs in White Rats inoculated with Murine Typhus Strains. A Pathological Study.** *Chinese Med. J. Peking.* 1952, Mar.-Apr., v. 70, Nos. 3/4, 105-14, 5 figs. on 2 pls.

"Evidence is presented which suggests strongly that paralysis of legs observed in white rats inoculated with murine typhus strains was due to typhus rickettsia and not to some unrecognized extraneous agent. A detailed pathological study is given to this syndrome in white rats which may prove of interest to workers in the field of typhus research."

PEREPÉREZ PALAU, F. Contribución al estudio geográfico y epidemiológico de la fiebre exantemática mediterránea. [**A Geographical Distribution and Epidemiology of Mediterranean Exanthematic Fever**] *Rev. Sanidad e Hig. Pública.* Madrid. 1951, July-Aug., v. 25, Nos. 7/8, 472-5.

In the province of Tarragon in Spain 112 cases of "Mediterranean exanthematic fever" were reported during the 8 years, 1941-48. [A more suitable name for the disease would be tick-borne typhus of the boutonneuse type.] More than half of the cases occurred in the district of Reus; the rest were from 5 other districts. Only 20 of the cases were in persons aged less than 21 years, 52 were in persons over 50 years of age. All the cases occurred during the 6 months, May to October, and 82 were in August and September, the period of greatest activity of the vector ticks. A "black eschar" occurred in 78.5 per cent. of the cases. The illness was usually mild, no mention is made of any death.

*John W. D. Megaw*

BAUSSAY, J. Fièvres exanthématiques par morsures de tiques. [**Two Cases of Tick Bite Fever**] *Bull. Soc. Path. Exot.* 1952, v. 45, No. 2, 166-9, 1 chart.

The author, from Oubangui, French Equatorial Africa, records two cases of exanthematic fever in adults, both associated with the presence of dogs; in one, the bite of a tick was certain, and in the other it was probable. Full clinical details are given and the symptomatology was characteristic.

Both patients were treated with terramycin capsules, in divided doses amounting to 2 gm. daily for 3 days. The fever and rash disappeared within 72 hours.

*H. J. O'D. Burke-Gaffney*

RAO, K. N. A. **A Case of Tick Typhus in Srinagar.** *Indian J. Med. Res.* 1951, July, v. 39, No. 3, 293-6, 1 chart.

HARRIS, B. P. **Q-Fever in Nairobi.** *East African Med. J.* 1952, Apr., v. 29, No. 4, 128-30, 1 chart.

Account of a case.

FELLERS, F. X. **An Outbreak of Q Fever. II. Treatment with Aureomycin and Chloramphenicol.** *U.S. Armed Forces Med. J.* 1952, May, v. 3, No. 5, 665-71, 1 fig. [10 refs.]

The author describes the results of the treatment of 25 patients whose attacks of Q fever have already been discussed from the clinical point of view [see this *Bulletin*, 1952, v. 49, 613]. The conclusion stated is that "both aureomycin and chloramphenicol were found to produce a dramatic therapeutic response"

The patients were divided into 4 groups. One group of 5 with mild symptoms and an average duration of 5.1 days was excluded. The remaining 20 patients, who were ill on admission, were divided into 3 groups one of which consisted of 7 untreated controls, another of 7 treated with aureomycin and the third of 6 treated with chloramphenicol. With aureomycin the total dosage was 9 or 11 gm. of which 0.25 gm. was given every hour for 4 doses, then 0.5 gm. every 6 hours. With chloramphenicol 0.5 gm. was given every hour for 4 doses, and then every 6 hours, the total dosage being 10 or 12 gm.

A marked symptomatic improvement was noticed within about 12 hours and the temperature fell to normal in 12-52 hours, the average period being 30 hours. The average total duration of the fever was 10.1 days in the control group; in the aureomycin group it was 7.6 days and in the chloramphenicol group it was 6.1 days. The system on which the cases were allotted to the different groups is not stated.

[A less favourable impression of the value of chloramphenicol is conveyed in the report by CLARK *et al.* in whose description of the clinical features of 180 cases in California it is stated that most of the severe attacks were treated with this drug for varying periods in daily doses of 2 to 4 gm. and that the response was "generally minimal or completely absent" (see this *Bulletin*, 1952, v. 49, 136).]

John W. D. Megaw

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## BARTONELLOSIS

PETERS, D. & WIGAND, R. Neue Untersuchungen über *Bartonella bacilliformis*. 1. Mitteilung: Morphologie der Kulturform. [New Observations on *Bartonella bacilliformis*. I. Cultural Morphology] *Ztschr. f. Tropenmed. u. Parasit.* Stuttgart. 1952, Feb., v. 3, No. 3, 313-26, 17 figs. [27 refs.]

The English summary appended to the paper is as follows :—

"Cultures of *Bartonella bacilliformis* were studied by light, phase contrast and electron microscopy.

"Young cultures show polymorphous organisms in the shape of short rods, scanty long rods or coccoid forms. Lodgment is solitary or chained or aggregated. They multiply by binary fission. In old cultures coccoid forms only are found. Unfixed specimens average 0.66 by 1.1 microns in size. Membrane and cytoplasm show up distinctly in electron microscopy, also flagella, which are hardly visible under the light microscope. Flagella have diameters of about 20 millimicrons and undulation phases of 0.95 microns. They often form bundles visible in phase contrast microscopy without staining. They rise from the cytoplasm, their arrangement being cephalotrichous. Up to 10 flagella were counted for each organism. Bartonellas from condensing water of young agar cultures showed rectilinear or torsional movements.

"*Bartonella bacilliformis* differs morphologically from *Bartonella muris*, *Eperythrozoon coccoides*, *Anaplasma marginale*, and resembles bacteria. Unlike rickettsias they are flagellated and cultivatable."

NAUCK, E. G. Elektronenoptische Darstellung von *Bartonella muris* Mayer. [Electron Micrography of *B. muris*] Reprinted from *Optik*. 1950, v. 7, 323-4, 2 figs.

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## YELLOW FEVER

JELLIFFE, D. B. **The Continued Presence of Yellow Fever in Ibadan, W. Nigeria.** *West African Med. J.* 1952, Apr.-May-June, v. 1 (n.s.), No. 2, 65-6.

Yellow fever protection tests carried out in Nigeria by BEEUWKES and MAHAFFY [this *Bulletin*, 1934, v. 31, 829] and SMITH and HOWIE [*ibid.*, 1943, v. 40, 303] showed that positive results were obtained in 42 per cent. and 11 per cent. respectively of 220 and 100 African schoolchildren in Ibadan.

To discover whether clinically unrecognizable yellow fever still occurred in Ibadan, the author carried out protection tests on 74 African children between 8 and 9 years old, who had thus been born since the last survey: none had been inoculated against yellow fever. There were 13 (17.6 per cent.) positive tests.

Clinical yellow fever is rare in Africans in the absence of an epidemic and only one case seems to have been recorded in an African in Ibadan in the last 20 years, and that by post-mortem examination of the liver. The author discusses the differential diagnosis and the likelihood of cases being unrecognized.

His own survey seems to indicate that yellow fever has continued to occur in Ibadan during the last 9 years, either in a permanently endemic form or in isolated outbreaks introduced from outside: the latter explanation is emphasized by the occurrence in 1946 of a small epidemic of yellow fever about 65 miles away from Ibadan; in this place, Ogbomosho, there were 49 cases and 11 deaths.

H. J. O'D. Burke-Gaffney

KUMM, H. W. **Periodicity in the Annual Incidence of Reported Cases of Yellow Fever during the Past Fifty Years.** *Amer. J. Trop. Med. & Hyg.* 1952, Mar., v. 1, No. 2, 210-19, 2 charts. [13 refs.]

Periodicity of incidence is a characteristic of many infectious diseases, including measles, influenza, cerebrospinal meningitis, malaria, and others. An indication of periodicity was noted in some records of yellow fever, and available data on annual incidence were therefore collected from case reports and viscerotomy returns. The reports of cases from Africa and South America date from 1900, and for each country show a series of peaks separated by intervals of which the commonest as well as the average duration is 6 years. Viscerotomy records since 1930 show a similar periodicity, and it is notable that for neither of them do the peak years in different countries coincide. The pattern is irregular but seems to show the periodicity common to many diseases. G. Macdonald

SOPER, F. L. **Yellow Fever in the Caribbean.** *Bol. Oficina Sanitaria Panamericana.* 1952, Mar., v. 32, No. 3, 197-205, 4 maps.

The author briefly recounts the history of yellow fever in the Caribbean area, whence the urban disease has disappeared since 1937 but where the jungle disease has recently recurred. The paper is illustrated by 4 maps which effectively illustrate the location of positive immune reactions among monkeys; the distribution of past and recent outbreaks of yellow fever; the air routes connecting the territories and the operation of the *Aedes aegypti* Eradication Programme.

G. Macdonald

FINDLAY, G. M. & HOWARD, E. M. **The Transmission of Neurotropic Yellow Fever Virus to Rats.** *Ann. Trop. Med. & Parasit.* 1951, Dec., v. 45, Nos. 3/4, 220-22.

White rats (strain not stated) up to 13 days of age were found to be susceptible to intracerebral (i.c.) inoculation of French neurotropic yellow fever virus. By

21 days of age the rats were resistant to infection by that route, as were rats of 2, 8 and 20 days which had been inoculated intraperitoneally. It is suggested that the change in susceptibility to i.c. inoculation with the virus is not due to the development of a blood-brain barrier, but that the change in metabolism during the first 3 weeks of extra-uterine life is associated with the change in susceptibility of young as compared with old suckling rats. G. W. A. Dick

ELTON, N. W. Histopatología renal en fiebre amarilla. [**Kidney Changes in Yellow Fever**] Reprinted from *Archivos Med. Panameños*. 1952, Jan., v. 1, No. 1, 41-9, 10 figs. [17 refs.]

The author has taken the occurrence of 4 fatal cases of yellow fever to describe and discuss the pathological changes seen in the kidneys. The chief of these are, of course, the degeneration of the tubule epithelium, the Councilman bodies and the Hoffman bodies. The colloid and crystalline bodies described by Councilman were seen in all 4 patients, as isolated or grouped masses, or, occasionally, in chain formation; they are hyaline but tend to show a darker centre, giving a "bull's eye" appearance. Some authorities maintain that they are by no means pathognomonic of yellow fever, since they occur after administration of sulphonamide drugs and in carbon tetrachloride poisoning and are indicative of liver damage. The lime casts of Hoffman were seen in one only of the 4 cases. All 4 showed haemoglobinuric nephrosis. These pathological changes are depicted in a series of [rather faintly reproduced] photomicrographs.

H. Harold Scott

## RABIES

LEVADITI, C., VAISMAN, A. & HENRY-EVENO, J. Symbiose entre le virus Coxsackie, souche encéphalitogène, et le virus de la rage des rues (souche Tanger). [**Symbiosis between an Encephalitogenic Strain of Coxsackie Virus and Rabies Street Virus (Tangier Strain)**] *Ann. Inst. Pasteur*. 1952, Apr., v. 82, No. 4, 499-502.

LEVADITI, C., VAISMAN, A. & HENRY-EVENO, J. Symbiose entre le virus Coxsackie, souche encéphalitogène, et le virus rabique fixe. [**Symbiosis between an Encephalitogenic Strain of Coxsackie Virus and Fixed Rabies Virus**] *Ann. Inst. Pasteur*. 1952, Apr., v. 82, No. 4, 502-5.

DAS, A. & ROY, S. K. **Terramycin in Rabies.** *Calcutta Med. J.* 1952, Mar., v. 49, No. 3, 112-13.

"Five cases of rabies were treated with intravenous injections of terramycin. The mortality and survival time was not influenced."

DARZINS, E. & BISMANIS, J. **Experience with the Antirabic Vaccination in the Two World Wars.** *Ztschr. f. Hyg. u. Infektionskr.* 1952, Feb. 29, v. 134, No. 1, 117-22.

Under war-time conditions it was not possible to produce enough vaccine from the central nervous systems of rabbits, and Pasteur's scheme of vaccination was found to be impossible to carry out. A sheep brain vaccine was made by ether extraction following Hempt's method: 367 persons were vaccinated with the sheep vaccine and 343 with Hempt's rabbit vaccine. Six injections each of 4 ml. were given to adults and half this dose was employed for children under 4 years. Thirty days after the sixth inoculation a seventh dose was given.



Of the total of 343 persons vaccinated with rabbit vaccine 3 died of rabies and none of the 367 vaccinated with the sheep vaccine died. On these results the authors abandoned the use of the rabbit vaccine in favour of the sheep-brain vaccine. [Even if the differences in the two groups had been significant the authors have not recorded that they took any precautions to randomize their samples. The number of variables which arise in the evaluation of the efficacy of rabies vaccine are numerous and are presented in detail by the late Professor GREENWOOD in the tenth statistical review of rabies (this *Bulletin*, 1947, v.44, 636).]

G. W. A. Dick

## PLAGUE

HEIM DE BALSAC, H., LE GAC, P. & GIROUD, P. Étude des rongeurs de l'Oubangui-Chari (A.E.F.). Détermination de certaines espèces susceptibles de représenter des réservoirs de virus. (Deuxième Note.) [Study of Rodents of Oubangui-Chari. Determination of Species Capable of Representing Reservoirs of Virus] *Bull. Soc. Path. Exot.* 1952, v. 45, No. 2, 212-17. [13 refs.]

KNUTSON, H. & SZYMKOWICZ, R. T. Ectoparasitism of Norway Rats in an Inland New England Village and in a New England Seaport. *J. Econom. Entom.* 1952, Apr., v. 45, No. 2, 338-9.

"Ectoparasitism data in the small inland village of Kingston, R.I., were obtained and limited comparison made with studies by Robinson in the large coastal city of Providence.

"In Kingston, *Nosopsyllus fasciatus* constituted 85 per cent of the flea population. It infested 41 per cent of the rats, averaging more than one per rat and four per infested rat. *Xenopsylla cheopis* was not taken in Kingston but made up 75 per cent of the Providence population. *C. pseudagyrtes* constituted the remaining 15 per cent of the Kingston population.

"*Haemolaelaps glasgowi* constituted 93 per cent of the Kingston mite population. It infested 30 per cent of the rats, averaging four per rat and thirteen per infested rat. The remaining 7 per cent was *Eulaelaps stabularis* which infested 11 per cent of the rats. Thirty-seven per cent of the rats were mite-infested. Providence collections were virtually all *E. echidninus*, infesting 21 per cent of the rats.

"*Polyplax spinulosa* was the only louse in both the Kingston and Providence collections. In Kingston it infested 81 per cent of the rats, averaging 25 per rat and 31 per infested rat. It infested 24 per cent of the rats in Providence.

"Certain data on combinations of the various species on individual hosts and maximum parasitism counts are given."

TANAKA, H., IKUZAWA, M. & MORIYA, S. [Medical Zoological Studies on the Rats in Osaka City (I)] *J. Osaka City Med. Center.* 1951, Oct., v. 1, No. 1, 20-26, 2 graphs. [26 refs.] [In Japanese.] English summary.

TANAKA, H., IKUZAWA, M., MORIYA, S. & SUMIYOSHI, K. [Medical Zoological Studies on the Rats in Osaka City (II)] *J. Osaka City Med. Center.* 1952, Jan., v. 1, No. 2, 101-5, 2 figs. [28 refs.] [In Japanese.] English summary.

POLLITZER, R. Plague Studies. 4. Pathology. *Bull. World Health Organization.* Geneva. 1952, v. 5, No. 3, 337-76. [129 refs.]

This is the 4th of the series of studies by the same author [this *Bulletin*, 1952, v. 49, 388, 616, 690]; when complete these will form a manual on plague.

which will be published by the World Health Organization. The present contribution is on the same plan as the previous papers and it maintains the same high standard of excellence. The pathology of plague is described under the following headings: Bubonic Plague in Experimental Animals; Pneumonic Plague in Experimental Animals; Natural Plague in Animals; Human Plague, Bubonic and Primary Pneumonic.

In discussing the classification of plague the author points out that no dividing line can be drawn between bubonic and septicaemic plague; he suggests that only two forms of the disease should be recognized: (a) bubonic plague including septicaemic and secondary pneumonic types, and (b) primary pneumonic plague, defined as the form in which infection enters through the deep parts of the respiratory system and in which the disease runs a very rapid course ending in death unless treatment by the newer potent drugs is given.

[The only objection to this simplified classification is that the name bubonic is hardly suitable for types of the disease in which buboes are absent or are incapable of detection. From the practical point of view the most important matter is to differentiate between plague transmitted to man from lower animals, nearly always by fleas, and plague transmitted from man to man, nearly always by inhalation of infected droplets. Suitable names for these two forms would be "zootic" and "demic" respectively; these names are obviously more suitable than epizootic and epidemic which indicate a high degree of prevalence of an infection among animals or human beings and so cannot be used to designate infection transmitted from animals or persons.]

John W. D. Megaw

## AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

HELLUY, J. R. & SCHWARTZ, J. L'amibiase autochtone dans l'Est. Histoire d'une épidémie. [**Autochthonous Amoebiasis in the East. History of an Epidemic**] *Rec. Travaux Inst. Nat. Hyg. Paris.* 1952, Tome 4, v. 2, 983-9.

In June 1948 an outbreak of febrile diarrhoea, some of it dysenteric in character, began in the area of Joeuf-Homécourt-Auboué in the Department of Meurthe-et-Moselle [N.E. France]. The outbreak increased in extent until August, when the appearance of some cases of amoebic liver abscess indicated that the epidemic was one of amoebic dysentery. Examination of pus obtained from abscesses showed the presence of amoebae, and some stool examinations proved the presence of an intestinal *Entamoeba histolytica* infection in some of the affected. Most of the sufferers had never been abroad and had not recently been away from the locality. The number of cases of dysentery was estimated to be about 1,000, and about 20 developed amoebiasis of the liver.

Enquiries were set on foot as to the origin and method of spread of the infection. The source was thought in part to be a small colony of North Africans living under squalid and miserable conditions, who indulged in promiscuous defaecation; and in part to be repatriated prisoners of war and others who in the past had suffered from dysentery elsewhere. The spread of the infection was facilitated by the primitive sanitary habits of the population, and their practice of using night soil as garden fertilizer.

Measures were advocated to control the latter practice, to forbid the use of possibly contaminated water for purposes which might promote the distribution of infection, and to ensure the cleansing of possibly polluted vessels and clothing, and the hands of those preparing food. They were effective in preventing a recurrence of the epidemic in the following years, when only isolated cases occurred.

A. R. D. Adams



LUBINSKY, G. **The Occurrence in Pakistan of a Human *Entamoeba* of the *polecki* Type.** *Parasitology*. 1952, Mar., v. 42, Nos. 1/2, 48-51, 9 figs.

The author describes the repeated finding in the stools of a healthy inhabitant of Pakistan of uninucleate amoebic cysts comparable to those described by KESSEL and JOHNSTONE under the name *Entamoeba polecki* [this *Bulletin*, 1950, v. 47, 43]. The person in question also harboured a variety of other amoebae, including *E. histolytica*. In discussing the nature of the *polecki* type of cysts found by him, the author points out that the stools contained typical uninucleate cysts of *E. histolytica*, as well as some in which the nuclear structure was intermediate between those of the latter and of the *polecki* type. It is suggested that, in the case described, a strain of *E. histolytica* was present in which the cysts, for some unknown reason, failed to develop beyond the uninucleate stage and finally degenerated, assuming the appearance seen in the *polecki* cysts.

C. A. Hoare

DOBELL, C. (The late). **Researches on the Intestinal Protozoa of Monkeys and Man. XII. Bacterial Factors influencing the Life History of *Entamoeba histolytica* in Cultures.** [Completed and edited by R. A. NEAL & C. A. HOARE.] *Parasitology*. 1952, Mar., v. 42, Nos. 1/2, 16-39, 1 fig. [10 refs.]

[This posthumous paper by the late Clifford Dobell was in manuscript form and unfinished when he died. Fortunately he kept daily records of his observations and these were used by Neal to reconstruct the missing part of the manuscript, and thus save this important work, upon which Dobell was engaged for 20 years, from oblivion.]

First a description is given of the method of cultivation of *Entamoeba histolytica* under anaerobic conditions, which are created in the tube by the aerobic bacteria present in the concomitant flora.

The author next turns to a general consideration of the rôle of the bacterial flora on the development of the amoebae in culture. Although it is a comparatively easy matter to cultivate the trophozoites of most strains indefinitely, many strains cannot be induced to encyst *in vitro*. The difference between encysting and non-encysting strains was thought to be due to their concomitant flora, a view which was confirmed experimentally. Many years ago Dobell isolated a strain of *E. histolytica* (K28c) which readily went through its entire life-cycle *in vitro*, and by substituting the concomitant flora of non-encysting strains by that of K28c he was able to convert them into good encysting strains. This success led to a bacteriological analysis of K28c and to attempts to grow various strains of *E. histolytica* with different combinations of bacteria constituting this strain, in order to ascertain the part played by each of them in the development of the amoebae. It was found that the K28c flora comprised 8 aerobic organisms (chiefly of the *Bacterium coli* group) and 6 anaerobes, the characteristics of which are described in detail.

The effects of individual species, and their combinations, were investigated by different methods. Firstly, by adding them to cultures of *E. histolytica* in excess or by hatching partly sterilized cysts in media previously "seeded" with the bacteria to be tested. Secondly, by sterilizing the cysts and then growing them in association with known bacteria. For sterilization, acriflavine and gentian violet were used. In the former case, cysts produced in a culture were repeatedly washed and allowed to settle in a test-tube, after which they were transferred to a tube containing 5-10 cc. of 0.1 per cent. acriflavine solution (1:1,000) and put in a refrigerator, where the suspension was left for a week or more. By this method all the aerobic bacteria of the flora accompanying the amoebic cysts are killed, but the spores of the anaerobes are not

affected. In order to eliminate the spore-bearing organisms, cysts of *E. histolytica* growing with a mixed flora are first treated with acriflavine, in order to kill the aerobes, after which they are induced to grow with a single aerobe (in addition to the anaerobes). Finally 1 cc. of a 0.1 per cent. solution of gentian violet is added to the culture, and daily subcultures with this dye are made, until the anaerobes are killed. By using these methods it was possible to produce "synthetic" strains of *E. histolytica* accompanied by any desired combination of bacteria, the properties of which it was desired to study.

The results of these experiments have shown that although the aerobic bacteria individually induced the cysts of *E. histolytica* to hatch and supported the growth of the amoebae indefinitely, they were unable to produce cyst-formation: the only species capable of promoting encystation was the anaerobe labelled *N*<sup>5</sup>. The chief rôle of the aerobic bacteria in the cultures is to provide the anaerobic conditions necessary for the growth of the amoebae with *N*<sup>5</sup>.

This is only a brief summary of a well-documented investigation, for details of which the reader is referred to the original paper. C. A. Hoare

NEAL, R. A. **Experimental Production of Pure Mixed Strains of *Entamoeba histolytica*.** *Parasitology*. 1952, Mar., v. 42, Nos. 1/2, 40-42. [11 refs.]

The author describes the results of experiments on the production of pure mixed strains of *Entamoeba histolytica*, with the methods devised by RAO [this *Bulletin*, 1952, v. 49, 268] and DOBELL [see above]. Among the strains used were two (*RD*, *XK*), isolated from rats experimentally infected with human strains, and Dobell's *K28c*. The bacteria used in these experiments were *Chromobacterium prodigiosum* and *Bacterium coli* [which will be referred to as *C.p.* and *B.c.* respectively]. In one set of experiments the cysts from cultures of *E. histolytica* were treated with chemicals by Rao's method, after which they were subinoculated in media seeded with *C.p.* and *B.c.*, in which they hatched and developed further. Repeated analyses of these cultures revealed the presence—in addition to the above-named aerobes—of anaerobic bacteria. In another set of experiments, Dobell's method of eliminating the spore-bearing organisms with gentian violet was employed, after Rao's method had been used for killing the aerobes in a culture of *RD* strain and the cysts from the latter were hatched in medium seeded with *C.p.* After 33 subcultures it was found that this strain was free of anaerobes, the only bacterial organism present being *C.p.*

The author thus successfully sterilized his cultures of *E. histolytica* by Dobell's method, but failed to eliminate the spore-bearing organisms by Rao's method.

C. A. Hoare

REARDON, Lucy V., VERDER, Elisabeth & REES, C. W. **The Cultural Requirements of *Entamoeba coli* and the Comparative Effects of Drying on the Cysts of *E. coli* and *E. histolytica*.** *Amer. J. Trop. Med. & Hyg.* 1952, Jan., v. 1, No. 1, 155-61, 2 figs. [10 refs.]

Cultures of *Entamoeba coli* were started from cysts in freshly passed and stored (15 days at 5°C.) stools. They were concentrated by a zinc flotation method in which narrow-necked tubes were used, and the cyst suspensions collected from the necks of 2 tubes were washed repeatedly in N/20 HCl and saline. The final sediment was resuspended in saline and transferred to a watch glass, where it was left to settle for 30 minutes. By inverting the watch glass, the faecal debris was eliminated, while the cysts remained adhering to the bottom. These were inoculated in whole egg medium with rice starch. The flora of the first culture contained organism *t* and *Geotrichium* but in subcultures a diphtheroid and *Bacillus subtilis* were also present. The following method was used for partial "purification" of the culture: a strip of sterile coverslip



was inserted into a mixed amoebic culture, left there for 72 hours of incubation, then withdrawn, passed through 4 tubes of sterile medium, and deposited in a 5th tube. By this means a culture was obtained of *E. coli* accompanied by 2 organisms—*t* and *B. subtilis*, which were thenceforth seeded into cultures with micro-isolated cysts in which a number of strains of *E. coli* were successfully grown. Encystation of *E. coli* was induced by Dobell's method: after cultivation without starch the amoebae are subinoculated into medium with starch. However, growth without starch could only be obtained by addition to the *E. coli*+*B. subtilis* mixture of at least one other organism, *Streptococcus zymogenes*, which was isolated from the flora of a strain of *E. histolytica*.

Experiments in the comparative effect of drying on cysts of *E. coli* and *E. histolytica* were carried out by drying the preparations in small drops of saline on sterile coverslip strips at a temperature of about 80°F. and relative humidity of 25–30 per cent., after which the strips were inoculated in microtubes with liver infusion agar medium, for tests of viability. It was found that cysts of *E. coli* survived drying and were capable of growing in culture, whereas those of *E. histolytica* were irreversibly injured and incapable of further growth.

C. A. Hoare

See also p. 911, ALICNA, **Stain for Endamoebas.**

FAUST, E. C. **Modern Criteria for the Laboratory Diagnosis of Amebiasis.** *Amer. J. Trop. Med. & Hyg.* 1952, Jan., v. 1, No. 1, 140–45.

The author gives an instructive outline of the laboratory diagnosis of infection with *Entamoeba histolytica*. Among the methods described are direct examination of fresh faecal smears in saline and iodine and the zinc sulphate technique for concentration of cysts. As regards the faecal specimens used in routine examination, it is emphasized that unformed stools, which might contain trophozoites, should be seen within a few minutes after evacuation, whereas formed stools may be safely kept for a day or two in a refrigerator, since the cysts remain unchanged. Formalin-fixed stools are not suitable for demonstrating the nuclear characters of the amoebae, but their diagnostic characters are not lost in faeces teased up with an equal amount of iodine stain (saturated I in 1 per cent. KI), while the polyvinyl-alcohol technique can be used in the preparation of faecal smears for subsequent fixation and staining. If there is a suspicion of amoebiasis but faecal examinations are consistently negative, specimens can be obtained after saline purgation (preferably with sodium sulphate or buffered phospho-soda) or enemas can be used. Among other methods, proctoscopic scrapings, aspiration (in extra-intestinal infection) and biopsy (during surgical exploration), as well as necropsy are mentioned. While both are useful under suitable conditions, the culture method and complement fixation are considered to be inferior to routine faecal examination for the diagnosis of amoebic infections. Finally, stress is laid on the importance of the human element in arriving at a correct diagnosis—the technical skill and experience of the laboratory worker, and the sound judgment of the physician.

Though dealing with recognized methods of diagnosis, this paper contains valuable hints and observations which will be appreciated by laboratory workers and physicians, who are referred to the original for detailed information.

C. A. Hoare

SCHORR, S. & SCHWARTZ, A. **The Roentgenologic Manifestations of Amebiasis of the Liver with Concomitant Findings in the Chest.** *Amer. J. Roentgenol. & Radium Therapy.* 1951, Oct., v. 66, No. 4, 546–54, 11 figs.

The early diagnosis of thoracic amoebiasis is of obvious importance. The progress of an amoebic abscess and its extension into the chest cavity can be

followed by radiological examinations. Forty-nine undoubted cases of liver amoebiasis have been studied by the authors during a period of 7 years ; 16 of these showed X-ray evidence of thoracic invasion ; in 2 of them the left as well as the right side of the chest was involved, in another case the left chest only was affected.

The first radiological changes in amoebiasis of the liver are enlargement of the liver shadow, raising of the right diaphragm, and restriction of its movement. Thoracic involvement is attended by obliteration of the costo-phrenic or cardio-phrenic sinuses, a pleural effusion, and pneumonic consolidation. In addition to deformation and fixation of the diaphragm a string-like linear perpendicular shadow often may be seen in the right lower lung field. This disappears after specific treatment ; it may be indicative of the spread of the inflammatory process, and its presence is suggestive of amoebic lung involvement. When X-ray lesions are found in the right chest in areas where amoebiasis is endemic, this condition should always be considered as their possible origin.

A. R. D. Adams

ANTONINI, F. Aspetti radiologici del tratto ileo-cecale nell'amebiasi cronica. [Radiological Changes in the Ileo-Caecal Area in Chronic Amoebiasis] *Arch. Ital. Sci. Med. Trop. e Parassit.* 1951, Dec., v. 32, No. 12, 1100-109, 4 figs. [28 refs.] English summary.

LUND, E. Enteritis caused by *Entamoeba histolytica* and *Giardia intestinalis*. *Acta Med. Scandinavica*. 1952, v. 142, Suppl. 266, 697-700. [18 refs.]

Symptomless autochthonous infections with *Entamoeba histolytica* occur in Scandinavia, as in other parts of the temperate climates. The spread of an *E. histolytica* infection in a temperate climate from persons infected in the tropics may result in intestinal symptoms. Two Norwegian students returned from a stay in Germany and Austria during which they suffered from diarrhoea with abdominal symptoms ; the symptoms persisted after their return, and examination of the stools showed the presence of infections with *E. histolytica* and *Giardia intestinalis* in both men. Both patients were cured symptomatically, and sterilized of their infections, by appropriate specific treatment.

A. R. D. Adams

ZAVALA, D. C. & HAMILTON, H. E. The Recognition and Treatment of Hepatic Amebiasis. *Ann. Intern. Med.* 1952, Jan., v. 36, No. 1, 110-25, 6 figs. [14 refs.]

"Seven cases of hepatic amebiasis are reported. Helpful diagnostic aids are (1) tender and often enlarged liver ; (2) fading suntan complexion of the skin ; (3) elevation or fixation of the right leaf of the diaphragm ; (4) little or no change in liver function tests ; (5) positive complement fixation test, with a fall in titer following specific amebicidal therapy, and (6) specific therapeutic response.

"Vioform, chiniofon, diodoquin, carbarsone, Milibis and two new thioarsenite derivatives of carbarsone oxide comprise the main list of amebicidal drugs which have a local action upon contact with the bowel wall. Favorable reports are appearing regarding aureomycin and terramycin, though they have not yet had adequate clinical trial. Chloroquine and emetine are the two drugs available for the treatment of extraintestinal amebiasis ; both drugs are specific for amoebic hepatitis and abscess. Chloroquine's high therapeutic effect and lack of toxicity render it superior to emetine. Chloroquine should



always be given *in combination with one of the local amebacidal drugs*, preferably diodoquin. Secondary infection should be treated with the appropriate antibiotic.

"The treatment of 28 patients with amoebiasis admitted to the hospital from 1938 through July, 1950, is reviewed. Two untreated patients died. Three out of a group of 15 patients treated with intermittent or alternating therapy had a total of seven relapses. There were no relapses in the group which received *combined therapy*."

ROOVERS, J. J. C. P. A. & VAN STEENIS, P. B. De behandeling van het leverabsces met chloroquine. [**Treatment of Liver Abscess with Chloroquine**] *Nederl. Tijdschr. v. Geneesk.* 1951, Nov. 10, v. 95 (iv), No. 45, 3316-26, 1 chart. English summary.

The English summary appended to the paper is as follows :—

"The authors present a general survey of the medicamentous treatment of the liver abscess and amoebiasis.

"The therapeutic result is determined by the efficacy of the medicament on the amebae and its concentration, on the spot where the amebae live, viz. in the intestinal wall, the liver and other tissues as histolytic forms, in the intestinal lumen as minuta-forms.

"In four patients, two of whom had become refractory to emetine, chloroquine acted rapidly and with good and lasting result, the patients not having had any relapse for 1½ to 2 years.

"Just as the emetine treatment of the liver abscess, chloroquine should be followed by a cure of yatrien or carbarsone in order to kill the minuta-forms in the intestinal lumen."

CROSNIER, R., DARBON, A., DUCOURNAU, P. & COSTEROUSSE, L. Le dibromhydrate d'amino-oxyconessine en thérapeutique de l'amibiase intestinale ou hépatique. Résultats obtenus. [**Amino-Oxyconessine Hydrobromide in the Treatment of Intestinal or Hepatic Amoebiasis**] *Bull. Soc. Path. Exot.* 1952, v. 45, No. 1, 86-92.

In view of the fact that treatment with conessine hydrobromide may be associated with the development of severe mental side-effects (though these are rare if the cases for treatment with the drug are carefully selected), its use has been confined to patients in hospital. It has not been considered suitable for domiciliary treatment.

A new and better-tolerated compound, amino-oxyconessine hydrobromide, has been prepared and has been under therapeutic test for a year. It has proved equally as effective as the early preparations of conessine against all forms of amoebiasis, both intestinal and hepatic. It does not give rise to any neuropsychological toxic complications, and so it can safely be used for the treatment of ambulant patients, thus much extending the range of the patients suffering from amoebiasis who can be given treatment with conessine.

A. R. D. Adams

BLANC, F. & MARTIN, M. Le traitement de l'amibiase hépatique aiguë par les iodiques solubles. [**Treatment of Acute Hepatic Amoebiasis with Soluble Iodized Compounds**] *Arch. Méd. Gén. et Trop.* 1951, July-Aug., v. 28, No. 4, 145-82, 15 charts.

After discussing the aetiology, manifestations, and diagnosis of amoebiasis of the liver the authors state that effective amoebicidal treatment of it during

the early stage, when there are only small disseminated islands of necrosis, is followed by restoration of the liver to normal. When the lesions have increased in size and coalesced, and there is a large collection of necrotic matter, drainage of this in addition to amoebicidal treatment is necessary to ensure rapid relief and an early return to normality. Both emetine and conessine are very effective diffusible amoebicidal drugs; they reach the foci of amoebic infection in the liver through the blood stream. But both drugs cause toxicity; that produced by conessine is immediate and severe; that due to emetine tends to be cumulative, so a repetition of emetine treatment may actually become dangerous. There is therefore much need for a diffusible amoebicidal drug, devoid of immediate toxicity and not cumulative, which will sterilize an amoebic infection of the liver.

Among the drugs effective in the eradication of intestinal amoebiasis are the iodo-oxyquinolines. These are contact amoebicides which act locally on the parasites in the bowel and are not absorbed to a material extent. Their therapeutically active constituent presumably is the iodine component; and certainly their activity is proportional to their iodine content. "Direxioide" (5-7-di-iodo-3-hydroxyquinoline), one of the latest and therapeutically the most effective of them, contains 69.9 per cent. of iodine. It therefore seems reasonable to determine whether absorbable and freely diffusible compounds with a high iodine content prove as effective in hepatic amoebiasis as do these non-absorbable compounds against the intestinal infection. Such diffusible compounds have for some time been employed in the treatment of visceral scleroses of vascular origin; the iodine content of the compounds employed as a rule is about 40 per cent., and so is about that of the oxyquinolines first used in intestinal amoebiasis. The following three compounds were selected for trial:—

1. "L'iodo-propanol-sulfonate de soude."
2. "L'iodo-benzo-méthyl-formine."
3. "L'iodohydrate d'hexaméthylènetétramine-éthanol."

Twenty-three patients suffering from acute and severe amoebic hepatitis were treated intravenously, and in a few cases orally, with one or other of these compounds over periods of 10 to 20 days. The particulars of each case in respect of the investigations made into it and its treatment with the selected iodine compound are set out at much length and in considerable detail. Twenty-one of the 23 patients who were considered to be suffering from presuppurative hepatitis, or at most very early abscess formation, were all cured by the iodine treatment. Two patients, both with well-developed abscess formation, were equally effectively cured of their amoebic infection of the liver, the necrotic matter being removed by aspiration in one case and by surgical drainage in the other. It was observed in all cases that the symptoms and signs had largely vanished at most by the sixth day of treatment. The therapeutic results equalled those obtained with the classical treatments with conessine or with emetine; and they were superior to these in view of the complete absence of toxic side-effects. No patient manifested any evidence of iodism as a result of the treatment. The authors have now adopted these diffusible iodine preparations for the routine treatment of amoebic hepatitis in their hospital practice. [See also this *Bulletin*, 1951, v. 48, 153.] A. R. D. Adams

WENGER, H. **Treatment of Chronic Intestinal Amebiasis with a New Oxyquinoline Compound.** *Indian J. Med. Sci.* 1952, Apr., v. 6, No. 4, 246-9.

Chronic intestinal amoebiasis is frequently met with in Southern Maharashtra and the author has had a year's trial of a new oxyquinoline compound in a large number of patients. The compound is 5,7-dichlor-8-hydroxyquinaldine



(Siosteran, V.R. 764) and was received from Messrs. Geigy of Basle. It is marketed in tablets of 0.1 gm. and the dosage used for adults was 2 tablets twice daily for 4-5 days. (It is added that the patients were mostly about one-third lighter in weight than Western Europeans.)

The present record refers to those cases only having stools clearly positive for *E. histolytica* or cysts before treatment and these amounted to 26. Unfortunately follow-up examinations were limited, as patients often did not return "which speaks in favour of their feeling recovered". However, in all cases at least one microscopic examination of stools was made after treatment, in 10 there were 2 and in 4 there were 3 such tests. On this basis, all 26 were negative after treatment, although one patient required 2 additional days' treatment for this result. In another, stools remained negative but amoebic hepatitis was also present: this responded to emetine. The cases are listed in detail in a table. No side-effects were observed. The author concludes that the results were satisfactory when compared with those "obtained with other preparations". It is pointed out that the absence of iodine in the preparation may be important for patients who are sensitive to this drug.

[The restricted parasitological follow-up in this small series limits the possibility of assessing the value of the drug.] *H. J. O'D. Burke-Gaffney*

MCVAY, L. V., JR. & SPRUNT, D. H. **A Long Term Evaluation of Aureomycin in the Treatment of Amebiasis.** *Southern Med. J.* 1952, Mar., v. 45, No. 3, 183-90, 5 figs. [19 refs.]

The authors [this *Bulletin*, 1949, v. 46, 1044] have stated that aureomycin is an effective amoebicide both *in vitro* and *in vivo*. This present paper is a report on 2 years' study of aureomycin in the treatment of amoebiasis. One hundred and fifty patients comprising both sexes and all ages have now been treated successfully for amoebiasis with 0.5 gm. of aureomycin by mouth 4 times daily for a week (a total of 14 gm. of the drug over 7 days). The diagnosis in each case was established parasitologically. In this series 16 patients were asymptomatic, 53 had "amoebic colitis", and 11 amoebic dysentery; there were 9 with amoebic hepatitis [80+9 patients]. The 80 patients with purely intestinal infections were under observation for at least 3 months after treatment. All of the 80 became asymptomatic and their stools were free from parasites at the end of the treatment; one month later parasites had reappeared in the stools of 7 of them; and after 3 months 3 others showed parasites. Of 52 of the apparently cured patients examined for a 6-month period, 3 showed parasitic relapse; of 42 of the residue seen for 9 months, one had a parasitic relapse; of 38 seen for 12 months, another one; and among 22 watched to 15 months there was no further relapse. The mode of examination was to recall patients to the clinic one month after treatment, and thereafter at 2- or 3-month intervals. On these occasions 3 stool specimens were examined directly, in stained specimens, and by a cultural method.

Nine patients had "clinical and laboratory evidence" of amoebic hepatitis; 7 of these had amoebic dysentery and 2 "amoebic colitis". In all these 9 there was liver enlargement with a derangement of the liver function tests. Aureomycin treatment produced resolution of the symptoms and signs, and a restoration of liver function. There were 2 cases of amoebic liver abscess, and these patients were successfully treated with a combination of chloroquine and aureomycin, with closed surgical drainage of the abscess cavity.

Amoebic appendicitis and caecal tenderness [which are referred to as common complications of amoebiasis] readily responded to aureomycin treatment. A case of cutaneous amoebiasis around a colostomy wound improved under aureomycin treatment, but did not finally clear until chloroquine also was given.

The side-effects of aureomycin treatment were : increased appetite (30 per cent.), transient nausea (14 per cent.), slight diarrhoea (9 per cent.), vomiting (5 per cent.), and pruritus (3 per cent.). Feelings of emotional tenseness and anxiety occurred in 3 per cent. of patients given the drug.

A daily oral dosage of 2 gm. of aureomycin produces an intestinal concentration of 50,000 to 100,000  $\mu$ gm. of the drug per gm. of liquid faecal material. These levels are from 50 to 100 times greater than are the lowest amoebicidal concentrations of aureomycin *in vitro* ; so it appears probable that aureomycin primarily exerts its action on the bowel infection directly on the amoebae, and that any effect on the intestinal flora is merely incidental in eradicating the infection.

The authors conclude that aureomycin is rapidly effective in all forms of amoebiasis, including amoebic liver abscess. A. R. D. Adams

ADAMS, A. R. D. **Amoebicides.** *Practitioner.* 1952, Apr., v. 168, No. 1006, 419-24.

A general review of the present position.

HANSEN, E. L. & BENNETT, B. M. **Effects of Toxic Agents on *Endamoeba histolytica*.** *Exper. Parasit.* New York. 1952, Mar., v. 1, No. 2, 143-56, 3 figs. [14 refs.]

The authors have made a study of sub-lethal doses of different chemical substances on cultures of *E. histolytica* accompanied by organism "t". Some of these substances have been used in the treatment of amoebiasis, two antibiotics, terramycin and bacitracin, as well as various chemical agents used in the treatment of cancer were also included in the study. Quantitative estimations of the number of amoebae present in the inoculum and after incubation were made in a haemocytometer. Besides the normal method of test with cotton-stoppered tubes, those sealed with petrolatum as described by BRADIN and HANSEN [this *Bulletin*, 1950, v. 47, 538] were also used. The culture medium was monophasic, consisting of liver-proteose-peptone with the addition of rice starch. The counts of amoebae were made in separate tubes at intervals up to 48 hours after inoculation so that neither control tubes nor those with drug should be disturbed. The drug was added immediately after the inoculum to give the desired concentration. It was concluded that the use of a dose response curve provided a valuable means of comparing the amoebicidal properties of different agents. By employing sub-lethal doses of drug synergic action between the different drugs could also be studied. It was noted in agreement with STEWART [this *Bulletin*, 1949, v. 46, 831] that during the early hours of contact of *E. histolytica* with emetine, the parasite was able to multiply but not in the presence of antibiotics which exerted lethal activity from the start, probably indirectly through antibacterial action. Viable amoebae, showing pseudopodial activity or movement of cytoplasmic granules, could usually be subcultured except after contact with certain concentrations of triethylene derivatives of cyanuric acid or after 24-hour contact with emetine, thioarsenite or vioform-soluble at concentrations which proved lethal after 48 hours. It is suggested that consideration of the factors investigated should lead to a better understanding of the chemotherapy of the infection.

J. D. Fulton

JONES, W. R. **Experimental Attempt to Induce Drug-Resistance in *Entamoeba histolytica*.** *Exper. Parasit.* New York. 1952, Mar., v. 1, No. 2, 118-28, 4 figs.

Claims for the development of strains of *E. histolytica* resistant to emetine have been made in the past [this *Bulletin*, 1931, v. 28, 268 ; 1939, v. 36, 304 ;



1940, v. 37, 115] but are not generally accepted as valid in view of the experimental conditions employed. The present author has re-investigated the possibility of producing strains resistant to the same drug by *in vitro* and *in vivo* techniques using young rats as hosts. In the *in vitro* experiments a simple liquid medium was used consisting of

sterile horse serum ... ..	0.5 ml.
1% Marmite* solution ... ..	1.0 ml.
buffered saline solution (pH 7.2) ...	8.5 ml.
rice starch ... ..	30 mg.

\*Marmite is an autolysed yeast extract made by Marmite Ltd., London.

The toxicity of different concentrations of emetine for 5 strains of *E. histolytica* (4 human and 1 monkey) was determined by culturing for 4 days at 37°C. in presence of serial dilutions of the drug. The inhibitory concentration for any one culture varied in the 8 experiments carried out over a period of 4½ months, and differences were apparent in the different cultures. In the attempt to produce resistance surviving amoebae from treated cultures were re-exposed to emetine by subinoculation into fresh medium with drug on 24 occasions over a period of 5 months. No increase in resistance was noted at the end of the experiment, but on the contrary the treated strain appeared to be somewhat more sensitive to emetine than the parent strain. In the *in vivo* experiments the intracaecal inoculation of young rats with *E. histolytica* from cultures was used as described by the author [this *Bulletin*, 1947, v. 44, 313]. Emetine was given orally at different dosage levels morning and evening on the 2 subsequent days, and the degree of infection was assessed when the rats were killed on the 5th day (day of infection being zero) by considering the number of amoebae and character of the intestinal lesions present. Attempts to produce resistance in the parasite were made by passage of surviving amoebae from the rat tissues to fresh animals which were also treated with drug and sacrificed in the same way. In this way 30 serial passages were made in 5 months and the strain was then inadvertently lost by death of the animals. The response to emetine in rats inoculated with 2 different cultures indicated that the doses required to produce a standard therapeutic effect varied in the two cases. The repeated passage of *E. histolytica* in rats exposed to non-curative doses of emetine also failed to induce resistance to the drug. J. D. Fulton

BERBERIAN, D. A., DENNIS, E. W., KORNS, R. F. & ANGELO, C. A. **Drug Prophylaxis of Amebiasis.** *J. Amer. Med. Ass.* 1952, Mar. 1, v. 148, No. 9, 700-704, 1 chart.

Amoebiasis is considered by many in the U.S.A. to constitute a serious epidemiological problem in institutions, especially mental hospitals. Its control lies in efficient faecal disposal and in reducing the incidence of the infection in the community by treatment.

Drugs which are most effective in sterilizing intestinal amoebic infections are mostly ineffective against extra-intestinal foci of infection. An intestinal infection may be cured without affecting an incipient hepatic infection. For efficient control therapy must be directed against both the intestinal and the extra-intestinal foci of infection. To this end Milibis (bismuth glycolylarsanilate) and chloroquine phosphate (aralen diphosphate) were combined in tablets containing 250 mgm. of the former and 75 mgm. of the latter. An institution containing 5,000 mentally defective patients was selected for a therapeutic trial of the tablets. Samplings of the population by stool examinations showed that 55 per cent. of the patients of low-grade mentality harboured *Entamoeba histolytica* infections, but only 17 per cent. of those of high-grade mentality

did so ; 4 per cent. of the employees engaged in the buildings were found to be infected.

Three hundred and ten patients of low mentality in two blocks of buildings were found to be infected with the parasite. They were divided into 5 intermingled groups for the purpose of an experiment. The first group had no treatment ; the others had varying courses of treatment with the tablets. It was found that 6 tablets of the drug combination by mouth daily for 7 days apparently sterilized the intestinal *E. histolytica* infection in 93 per cent. of those treated with it ; the subsequent prophylactic administration of 6 tablets at weekly intervals kept their infection rate down to 25 per cent. in highly infective surroundings over a 3-month period of observation ; a daily dose of 2 tablets kept it down to 10 per cent. under similar conditions ; whereas in a control group receiving no drug prophylaxis the incidence of infection during this period was 76 per cent. No toxicity attended the use of the tablets. This means of chemoprophylaxis is advocated as being particularly suitable for the tropics, where the chloroquine constituent of the tablets would be effective also against malaria.

[See also this *Bulletin*, 1952, v. 49, 771.]

A. R. D. Adams

NEGHME, A., AGOSIN, M., CHRISTEN, R. & RUBIO, Mafalda. *In vitro Action of Aureomycin and Terramycin on Balantidium coli*. *Exper. Parasit.* New York. 1952, Mar., v. 1, No. 2, 189-95.

The effect of aureomycin and terramycin on *Balantidium coli* in culture has been briefly reported by the authors [this *Bulletin*, 1951, v. 48, 156, 471, 1114] and favourable results with the first named substance are stated to have been obtained in 4 patients with this infection for which no satisfactory treatment is so far known. The organism was obtained from a dysenteric patient and cultured in a diphasic medium of coagulated blood serum overlaid with rabbit serum in saline plus some rice starch of pH 7.5 at a temperature of 37°C. Penicillin and streptomycin were used to inhibit the accompanying bacteria. After the parasites had been counted aureomycin and terramycin were added to the culture and the former, which is not stable at the pH employed, again at 24 and 48 hours to give the desired concentration. The effect of penicillin and streptomycin on *B. coli* was found to be negligible. The possibility of a synergic action between these substances and the other two antibiotics was also ruled out. It was concluded that both aureomycin and terramycin acted directly on *B. coli* and not on the accompanying bacteria. The effective concentration of each drug was approximately 0.4 mgm. per ml.

J. D. Fulton

## RELAPSING FEVER AND OTHER SPIROCHAETOSSES

KALRA, S. L. & RAO, K. N. A. **Observations on the Epidemiology of Relapsing Fever in Kashmir.** *Indian J. Med. Res.* 1951, July, v. 39, No. 3, 319-21.

"An appreciable density of *O. tholozani* var. *crossi* influencing the incidence of relapsing fever starts from the foothills of Jammu Province and extends into the Kashmir valley, but rapidly diminishes in Ladakh. The breeding season of the ticks does not appear to influence the incidence of the disease."



KALRA, S. L. & JACOB, V. P. **Effect of DDT and BHC on *Ornithodoros* Ticks.**  
**Part II.** *Indian J. Med. Res.* 1951, July, v. 39, No. 3, 311-17.

"In field trials BHC was more effective than DDT in eradicating ticks and its effect was more lasting. On large-scale application DDT failed to control relapsing fever, while BHC reduced its incidence considerably."

TEESDALE, C. **The Control of *Ornithodoros moubata* (Murray) with 0.5 per cent Gammexane Insect Powder (D.034) at Golini, Kwale.** *East African Med. J.* 1952, Apr., v. 29, No. 4, 138-41.

*Ornithodoros moubata* is widely distributed along the coastal belt of Tanganyika and Kenya; relapsing fever is endemic among the African population in certain districts, notably the Shimba hill country south of Mombasa; there mean annual temperatures approximate 69°F. minimum and 83°F. maximum and the annual rainfall is between 40 and 50 inches. The peasantry live in the usual type of African houses with mud walls, earth floor and palm-leaf thatch; goats and chickens share these houses with the occupants.

In this field experiment 80 houses were chosen indiscriminately and examined for the presence of ticks; numbers were summarized to give the average catch per house and to group the houses according to catches, *viz.*, nil, 1-10, 10-20, 20-30, 30-40, over 40: 25 houses were negative, 29 were in the 1-10 category and the remaining houses were evenly divided among the other categories; 6 houses in the over-40 category had an actual average catch of 66.3 ticks. Fifty houses were then treated with 0.5 per cent. gammexane powder by the simple method of sprinkling the powder from a perforated tin on to the cleared floor; the dosage was about 3.2 lb. per 1,000 sq. ft. The tabulated results indicate searches for ticks at intervals of 10 days, 1 month, 2 months and 3 months after dusting; in the control houses there was an increase in the average catches over the 3 months; in the treated houses there was a steady fall in the average catch until at 3 months all but two houses were free of ticks. The author accepts this period of 88 days as the time necessary between dusting and eradication. The catch figures are based on searches made by digging into earth floors to a depth of 5 to 6 inches, special attention being paid to the foot of walls, roof support posts and the feet of bedsteads.

By laboratory methods it was found that earth from the floors of treated huts remained lethal to ticks for 50 days. As eggs are unaffected by gammexane, nymphs may emerge after this period so that two or more applications at 3-month intervals may be necessary in the field to ensure complete eradication; however, there was an 84.4 per cent. decrease in the tick population in this field experiment within 10 days.

R. Ford Tredre

ANNECKE, S. & QUIN, P. **Relapsing Fever in South Africa: its Control.** *South African Med. J.* 1952, May 31, v. 26, No. 22, 455-60, 2 figs. [17 refs.]

African relapsing fever caused by *Sp. duttoni* transmitted by the tick *Ornithodoros moubata* occurs infrequently in the Union of South Africa, but sporadically in the Transvaal and along the east coast. Decentralization of expanding industry to the neighbourhood of African reserves in the warmer regions might result in markedly increased incidence of relapsing fever to the extent of interference with such agricultural or industrial projects. The prevalence of the disease was brought to the notice of the authors by the presence of spirochaetes in blood films taken in the course of malaria surveys; foci of tick harbourage became obvious in the North Transvaal. Investigation revealed large tick concentrations but little disease. The breeding places are

no different from those previously described elsewhere in Africa, namely, the dust and cracks of mud floors and similar crevices in walls or thatch of human dwellings. The quoted list of additional and unusual habitats associated with animals and rodents indicates that the tick is not entirely domestic. Migrant labour from tropical Africa introduces the spirochaete to tick-infested villages and industrial estates.

In the past, palliative control by burning of huts where relapsing fever occurred and the catching of ticks by varied and ingenious means in all dwellings proved uneconomical; eventually at the instigation of the Government Health Department the "building out" of the tick by cement and steel construction of dwellings proved to be effective and brought the additional benefit of improved social welfare. (Plans and specifications are included.) This permanent measure is costly and not applicable at present to rural villages. In consequence, experimental work was conducted with DDT and BHC; a single application of BHC wettable powder at 600 mgm. gamma-isomer/sq. ft. was lethal for 3 weeks, after which ticks reappeared and survived. A further field experiment, in which the same dosage was applied with the use of an emulsion of 17 per cent. BHC with 4 per cent. gamma-isomer, attained eradication; observations were maintained for a year after the single application. Further experiments demonstrated 300 mgm. gamma-isomer/sq. ft. to be the minimum dosage for eradication. The details of these experiments indicate that control with insecticides is "tiresome and tedious". Ticks may lie up for months until forced out by hunger, suggesting some sort of repellent action.

"Whatever method of extermination is decided upon is largely governed by financial considerations, it being borne in mind that one is permanent and the other requires constant attention with residual insecticides. Both yield results reflected in an economic and social improvement of the people."

[Hygienists are inclined to be "insecticide-minded" to-day and it is refreshing to read the insistent views of the authors that "permanent" measures yield the best and most economical long-term results, with lasting effect on social welfare also.]

R. Ford Tredre

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## LEPROSY

REV. BRASILEIRA LEPROLOGIA. S. Paulo. 1951, Dec., v. 19, No. 4, 255-70.  
III<sup>a</sup> Conferência Pan-Americana de Lepra (Realizada em Buenos Aires, 9-15 de dezembro de 1951). [Panamerican Leprosy Conference (Held in Buenos Aires, 9-15 December, 1951)]

Among the subjects discussed was that of classification, and the following was suggested:—

*Lepromatous type*.—Macular, diffuse, nodular, neural and systemic.

*Indeterminate group*.—Macular, neural and maculo-neural.

*Tuberculoid type*.—Macular, "*figurada*" (a term applied to the form with the raised margin and flat centre), neural and reactional.

Another important finding was with regard to changes occurring in cases in their reaction to the lepromin test. Positive reactors have exceptionally become negative. Under certain conditions (administration of sulphones, BCG, etc., and after repetitions of the lepromin test) negative or doubtful cases have become positive. This change has been noticed in the lepromatous type in very few cases and with only very low positivity. The same "positivization" has been provoked in the same ways in people without



leprosy. It was agreed that the administration of BCG was responsible for the largest proportion of changes of the lepromin test from negative to positive. In view of this it was agreed that the use of BCG should be generalized so as to determine definitely its value in leprosy.

*Ernest Muir*

HENS TIENDA, L. & FERNÁNDEZ NAFRIA, A. Epidemiología, lucha social y profilaxis de la lepra. [**The Epidemiology, Social Campaign and Prophylaxis of Leprosy**] *Med. Colonial*. Madrid. 1952, May 1, v. 19, No. 5, 462-83, 3 figs. [19 refs.]

This article brings up to date the results of efforts in recent years to deal with leprosy in Spain. The census made by CORDERO SOROA in 1948 [this *Bulletin*, 1951, v. 48, 813] gave 1,510 cases of the disease and 6,344 contacts who were under inspection. These numbers have now risen to 2,243 cases and 10,682 contacts. There are at present in existence or under construction buildings with 1,600 beds for the accommodation of leprosy patients in Spain. These are in the following places: Fontilles 400, Trillo 300, Toen 200, Tenerife 500, Las Palmas 100, Santiago 40, Barcelona 30, Granada 30. It is hoped that by the time of the International Leprosy Congress in Madrid in October 1953 there will be 2,500 beds, the number considered adequate to deal with the situation. The article ends with a warning as to the danger from well-to-do patients, with many bacilli, who undertake to isolate themselves at home, but because of a number of social and other complications are apt to make contacts and spread the disease. The authors consider that all open cases should be isolated in institutions.

*Ernest Muir*

LOWE, J. **The Leprosy Research Unit, Uzuakoli, Eastern Nigeria.** *West African Med. J.* 1952, Apr.-May-June, v. 1 (n.s.), No. 2, 67-71.

HUMPHRY, A. H. **Leprosy among Full-Blooded Aborigines of the Northern Territory.** *Med. J. Australia*. 1952, Apr. 26, v. 1, No. 17, 570-73, 1 fig.

It is stated that leprosy did not exist in the Northern Territory of Australia until introduced by Chinese coolies about 1874. But it remained confined to the Pine-Creek-Burrundie area till 1912 when the strict intertribal barriers among the aborigines was removed. During the war the leprosy control arrangements broke down under the threat of invasion, the leprosarium being closed and the patients returning to their own homes, so that during the last decade there has been a considerable increase in leprosy.

Leprosy is almost entirely confined to the northern half of the territory, that is north of 19th parallel, which has a humid, tropical climate. In this area there are 7,140 full-blooded aborigines, 4,181 of whom have been examined for leprosy, and 264 cases found. It is calculated that when the survey is finished some 400 cases in all will be found. Most of these people "are now living at missions, native settlements or cattle stations, crowded together in tiny 'humpies' devoid of windows or ventilation of any kind". The fairly high proportion of lepromatous cases, the want of sanitation and the frequency of hookworm are given as some of the other causes for the rapid spread of the disease.

In order to control leprosy, surveys are being made, and all open cases are segregated in the Channel Island leprosarium which is on an island 7 miles from Darwin. Also housing and dietary conditions are being improved. In carrying out segregation persuasion is used as far as possible in place of compulsion.

The incidence in various localities is shown, varying from nil up to 147·0 per thousand. The proportion of lepromatous cases is 49·3 per cent. Patients were till recently treated with sulphetrone at £13 per patient per year. The cost has now been lowered to £1 by using DDS. The criteria for discharge from the leprosarium are : the patient must have shown uninterrupted progress for 12 months, consistently negative smear findings for the next 12 months, and be in good physical condition ; he must be accessible for re-examination, and go to an area where he will be properly looked after if he is ill, preferably at a mission or settlement with a nurse in attendance.

Ernest Muir

PESCE, H. *Lepra en el Peru precolombino*. [**Pre-Columbian Leprosy in Peru**] *Rev. Brasileira Leprologia*. S. Paulo. 1951, Dec., v. 19, No. 4, 227-42. [107 refs.]

Although the study of historical records, and especially of Incan and pre-Incan remains, reveals the presence of other diseases such as syphilis, verruga and leishmaniasis, there is no indication of anything that can be interpreted as relics of leprosy prior to the arrival of Columbus. At the time of the discovery of America leprosy was a common disease in Spain, and the presumption is that the disease was introduced by the Spaniards. However, further investigations should be carried out, microscopic, macroscopic and radiological, to see if there are any changes in embalmed bodies which might indicate the existence of leprosy.

Ernest Muir

MALFATTI, M. G. **Study of the Morphology of *Mycobacterium leprae* under the Electron Microscope**. *Internat. J. Leprosy*. New Orleans. 1952, Jan.-Mar., v. 20, No. 1, 95-104, 1 text fig. & 9 figs. on 2 pls.

[See this *Bulletin*, 1951, v. 48, 1119.]

BOENJAMIN, R. **A Study of Vitamin A and Carotenoids and of Vitamin C in the Blood Serum of Leprosy Patients and of their Healthy Housemates**. *Internat. J. Leprosy*. New Orleans. 1952, Jan.-Mar., v. 20, No. 1, 53-66. [14 refs.]

[See this *Bulletin*, 1951, v. 48, 1122 ; 1952, v. 49, 57.]

FLOCH, H. & DESTOMBES, P. **Caséification et calcification des nerfs dans la lèpre tuberculoïde**. [**Caseation and Calcification of Nerves in Tuberculoïd Leprosy**] *Arch. Inst. Pasteur de la Guyane et du Territoire de l'Inini*. Publication No. 238. 1951, Aug., 4 pp.

The following is a translation of the authors' summary :—

In conclusion, we report a rare observation of calcification of the cubital nerve in a case of tuberculoïd leprosy : this calcification is the last stage of a caseous process commonly described as "nerve abscess", which is specific to tuberculoïd leprosy and is itself rare. [See also this *Bulletin*, 1935, v. 32, 336.]

H. J. O'D. Burke-Gaffney

MØLLER-CHRISTENSEN, V. & FABER, B. **Leprous Changes in a Material of Mediaeval Skeletons from the St. George's Court, Naestved**. *Acta Radiologica*. 1952, Mar.-Apr., v. 37, Nos. 3/4, 308-17, 11 figs. [10 refs.]

"A study of 200 skeletons from a Danish mediaeval leper churchyard revealed in about half, leprous changes of the same character as those found in contemporary lepers. In addition, the writers describe specific leprous—hitherto



unrecognized—cranial changes: 'facies leprosa', characterized by disappearance of the anterior nasal spine and of the alveolar processes corresponding to the upper incisors."

PORTUGAL, H. Notas à margem de uma publicação: Caso de lepra aguda maligna, com infecção do cônjuge em três meses de vida matrimonial, pelo Dr. H. C. de Souza Araújo—Mem. do Inst. Oswaldo Cruz, 48: 51 (1950). [Marginal Notes on an Article: "Case of Acute Malignant Leprosy with Conjugal Infection after Three Months of Married Life", published by Dr. H. C. de Souza Araújo] *Anais Brasileiros Dermat. e Sifil.* 1950, Dec., v. 25, No. 4, 235-42, 9 figs.

Histological examination was made by Dr. Portugal of biopsies from this peculiar case on 3 occasions with seemingly contradictory results [see this *Bulletin*, 1951, v. 48, 647]. On the first occasion it was reported as a reacting tuberculoid with innumerable bacilli; on the second as a tuberculoid granuloma (sarcoid type) with absence of bacilli; and on the third as lepromatous leprosy with innumerable bacilli. The explanation of these seemingly contradictory reports is that the case was one of the kind described by WADE and RODRIGUEZ as "Borderline tuberculoid leprosy" in which appearances of tuberculoid and lepromatous leprosy are found side by side in the same case. The paper is illustrated by 9 photomicrographs. [Cases of this nature are becoming more and more widely recognized throughout the world.]

Ernest Muir

SOUZA CAMPOS, N. Reação leprótica. Reação leprótica tuberculóide e lepra tuberculóide reacional. [Lepra Reaction. Tuberculoid Lepra Reaction and Reacting Tuberculoid Leprosy] *Rev. Brasileira Leprologia.* S. Paulo. 1951, Dec., v. 19, No. 4, 249-54.

[A distinction is made between these two forms of leprosy which is difficult for the average leprosy worker to follow.] Tuberculoid lepra reaction describes a case which shows an acute reacting appearance from the beginning, whereas reacting tuberculoid leprosy is a reacting phase in the course of the ordinary tuberculoid. Besides these two, and allied to both the reacting tuberculoid and the lepromatous form, is the so-called "border-line case".

Ernest Muir

SAMPAIO, S., DE SOUZA LIMA, L. & NAHAS, Linda. Corticotropin (ACTH) in the Treatment of Lepra Reaction. *Arch. Dermat. & Syph.* 1952, May, v. 65, No. 5, 617-19.

"Six patients with lepromatous leprosy, who had recurrent attacks of lepra reaction while receiving sulfone therapy, were subsequently treated with corticotropin (ACTH). The course of treatment varied in length from 4 to 34 days. All patients showed improvement in their general condition during the treatment. In one case there was a pronounced and immediate relief of the joint pains and neuritis, with some improvement in the cutaneous lesions. In the other cases no change in the skin lesions was noted. All cases were observed for a period of six months after the course of corticotropin. The hormone may be helpful in lepra reaction. The use of large doses given over a longer period, together with sulfone therapy, should be investigated."

FLOCH, H. & LECUILLER, A. Peut-on considérer une posologie-retard de la Diamino-diphényl-sulfone administrée par la voie buccale dans le traitement de la lèpre ? [**Can we Consider the use of Widely-Spaced Oral Doses of Diamino-Diphenylsulphone in the Treatment of Leprosy ?**] *Arch. Inst. Pasteur de la Guyane et du Territoire de l'Inini*. Publication No. 237. 1951, Aug., 7 pp. [11 refs.]

The authors give 3 tables showing the blood and urine concentrations after, respectively, 400, 600, and 800 mgm. of DDS had been given orally. After 400 mgm. there was only a trace in the blood on the third day and from 1 to 3.5 mgm. per cent. in the urine ; after 600 mgm. there was an average of 0.05 mgm. per cent. in the blood and 2.6 mgm. per cent. in the urine on the fifth day, and only a trace in each on the sixth ; after 800 mgm. there was an average of 0.42 mgm. per cent. in the blood, and from 3.1 to 7.6 mgm. per cent. in the urine on the 7th day, and 0.2 mgm. in the blood and from 1.2 to 5.3 mgm. per cent. in the urine on the eighth day. The authors found that 800 mgm. once a week was well tolerated provided that this dose was gradually reached by slow stages, starting with 50 mgm. once a week. This might if necessary be alternated with injections of 1.2 gm. of DDS in 10 cc. of a 2 per 1,000 agar-saline solution given once a week.

Ernest Muir

FLOCH, H. & HORTH, R. Intérêt de l'amide nicotinique dans les intolérances aux sulfones et le traitement des réactions léprotiques. [**The Usefulness of Nicotinic Acid in Intolerance to Sulphones and in Lepra Reaction**] *Arch. Inst. Pasteur de la Guyane et du Territoire de l'Inini*. Publication No. 243. 1951, Oct., 5 pp.

The authors mention 3 principal difficulties met with while using sulphones in the treatment of leprosy : the formation of a threshold of improvement which is difficult to pass over ; the small action of the sulphones on nerve lesions, especially in tuberculoid cases ; and the frequency of reactions especially at the beginning of treatment. They have found these difficulties overcome most effectively by the use of the anti-pellagra vitamin. It is particularly useful in lepra reactions which may either be averted before they occur or controlled after they occur. This vitamin can be given either in tablet form, or, for averting reactions, by injection.

Ernest Muir

PUPO, J. de A. Contrôle de endemia leprosa. (Bases atuais da luta contra a lepra). [**Control of Leprosy (Current Basis of the Fight against Leprosy)**] *Rev. Brasileira Leprologia*. S. Paulo. 1951, Dec., v. 19, No. 4, 203-13, 222-6, 6 graphs. [English version 214-21.]

A summary is given of the methods adopted in the State of São Paulo for the control of leprosy as the result of many years of experience. The campaign is divided under 8 departments : Epidemiological Investigation, Sanitary Control of Home Contacts, a Modified form of Compulsory Segregation, Care of Child Contacts, Preparation of Medicaments, Scientific Research, Teaching about Leprosy at Medical Schools, Social Assistance, and Sanitary Education. Leprosy is a very serious problem in the state of São Paulo as is shown by the numbers of patients recorded in the following years : in 1935, 1,817 ; in 1940, 1,541 ; in 1945, 1,297 ; and in 1950, 2,100. The percentages among these of lepromatous cases in each of these years were respectively 63.37, 55.10, 59.20 and 49.38. The article is illustrated with a number of graphs and charts.

Ernest Muir



FLOCH, H. Sur la vaccination par le B.C.G. en prophylaxie antilépreuse. Étude de la paraimmunité et de la para-allergie entre lèpre et tuberculose. [On Vaccination with BCG for the Prophylaxis of Leprosy. A Study of Para-Immunity and Para-Allergy between Leprosy and Tuberculosis] *Arch. Inst. Pasteur de la Guyane et du Territoire de l'Inini*. Publication No. 249. 1951, Dec., 14 pp. [18 refs.]

One hundred and forty-four patients were chosen, of whom 40 were lepromatous, 58 undifferentiated, and 46 tuberculoid. These were inoculated with two antigens, one of lepromin diluted 1/750 and the other of live BCG, diluted to contain a similar number of organisms. Of the 46 tuberculoids, 43 were positive to both, 2 were BCG positive and Mitsuda negative, and 1 was negative for both. Of the lepromatous cases 26 were negative for both, 12 were BCG positive and Mitsuda negative, and 2 were positive for both. Of the undifferentiated, 33 were positive for both, 10 negative for both, 14 BCG positive and Mitsuda negative, and one was Mitsuda positive and BCG negative. It is concluded that *Myco. tuberculosis* is able to bring about a condition of para-allergy *vis-à-vis* *Myco. leprae*, and the latter to a less extent para-allergy *vis-à-vis* the former, but only whole tubercle bacilli and not products of bacilli (as in tuberculin) must be used. Both bacilli are able to create between them conditions of crossed para-allergy and para-immunity, but *Myco. leprae* to a less extent than *Myco. tuberculosis*.  
Ernest Muir

## HELMINTHIASIS

GERBER, J. H. **Bilharzia in Boajibu. Parts I & II.** *J. Trop. Med. & Hyg.* 1952, Mar. & Apr., v. 55, Nos. 3 & 4, 52-8 ; 79-93, 1 fig., 1 plan & 4 charts. [15 refs.]

Although not so stated in the title or in the text, this valuable paper—which was awarded the Langley Memorial Prize—is confined to an account of urinary schistosomiasis. Throughout the paper, with one exception, the causal organism is referred to as *Bilharzia haematobium* ; the exception referred to is on page 55 when the more usual name, *Schistosoma haematobium*, is applied.

The village of Boajibu lies by the River Sewa, in the heart of what is believed to be the endemic area of schistosomiasis in Sierra Leone. Boajibu has a population of some 1,200 persons, and there are 8 smaller villages in the area, whose population varies from between 60 and 500.

The probable molluscan hosts in the area were considered to be *Bulinus* (*Physopsis*) *globosus* and *Bulinus* (*Physopsis*) *africanus*, while possible hosts were *Bulinus forskali* and *Lymnaea nyanzae*. Out of 204 shells sent to the British Museum 200 were identified as *B. africanus* and only 4 as *B. globosus*. Earlier workers in Sierra Leone regarded *B. globosus* as the more common snail, and the author thinks that this difference between their findings and his may be due either to the *B. globosus* population having increased or, as seems more likely to the reviewer, to the snails having been submitted for identification to different conchologists.

In places which nearly or entirely dried up, the number of molluscs decreased early, gradually at first, fairly rapidly towards the end. *Bulinus* does not tend to bury itself deep in the mud during the dry season, and attention is drawn to the possibility that new generations are preserved by the survival of the spawn. *Bulinus* occurs in greatest concentrations close to villages, and BLACKLOCK and THOMPSON [this *Bulletin*, 1924, v. 21, 940] refer to it as "quite definitely a sewage snail, and that to a marked degree", while RANSFORD [this *Bulletin*,

1948, v. 45, 618], who worked in East Africa, stated that *B. globosus* required "fouling of its habitat for its survival". A Boajibu *Bulinus*, although occurring close to villages, showed no association with urinary or faecal contamination of the water in which it occurred.

A total of some 600 snails from 6 different localities was dissected and the infection rate was found to vary from 0 to 46 per cent. These wide variations are not surprising when it is realized that the snails were collected from water supplies which varied greatly as regards the amount of water present and the rate of its flow.

To estimate the infection rate and the intensity of infection in the human population in different areas, morning specimens of urine were examined. The examinations were carried out either by direct search of the sediment with a microscope, or by adding water to the urinary specimen and watching with a hand lens for the presence of hatched miracidia. Altogether 1,855 urines were examined microscopically, or by both methods simultaneously, and 1,222 or 65 per cent. found positive, the incidence varying from 48 to 85 per cent. in the 9 villages investigated. The results of these examinations are set out in tables and in an interesting series of graphs, and the conclusion is reached that the incidence and intensity of the infection, and the viability of the ova, when investigated in communities grouped according to their proximity to the snail host, are closely related to each other, and that the incidence and intensity at least reflects accurately the extent of the snail and man contact.

As a result of his observations the author believes that a factor "loosely referred to as immunity" plays a predominant part in determining the intensity of the infection, as observed in the adult population. The following quotation is from the end of the carefully reasoned argument: "Perhaps the most favourable conditions to produce maximum protection are a moderate initial infection followed later on by regular 'booster doses' such as may be incurred by occasional exposure during one transmission period, and followed by an interval lasting to the next season, a sequence of events not likely to be commonly met with, but such as might conceivably take place in people living in villages remote from the snail host. All one can conclude with some degree of certainty is that immunity develops only if initial and early superinfection are of a limited, and closely correlated nature, and that the degree of protection conferred, the time needed to reach maximum efficiency, and its duration depend on the relative strength of these two factors.

"On the other hand, the worst possible combination of factors is easy to imagine—heavy initial infections with increasingly stronger subsequent ones, together with exposure at practically any time of the year—might result in early and extensive pathological changes in the host preventing the building up of an effective resistance, and that is possibly what happens in Egypt, to judge by the vast numbers of the snail host, the system of perennial irrigation and last, but not least, the disastrous effects of the infection on the human organism reported from that part of the world."

R. M. Gordon

MEHLMAN, B. & VON BRAND, T. **Further Studies on the Anaerobic Metabolism of some Fresh Water Snails.** Reprinted from *Biol. Bull.* 1951, June, v. 100, No. 3, 199–205, 1 fig.

PESSÔA, S. B. & COUTINHO, J. O. Considerações sobre os hospedeiros intermediários do *Schistosoma mansoni* no Brasil. [**On the Intermediate Hosts of *Schistosoma mansoni* in Brazil**] *Folia Clin. et Biol.* S. Paulo. 1950, Dec., v. 16, No. 2, 123–41, 8 figs. [32 refs.]

Of the 10 genera of the subfamily of Planorbidae two only are of medical importance, the large-shelled *Australorbis* and the small-shelled *Tropicorbis*.



Two species of the former are of importance in Brazil, viz., *A. glabratus* and *A. olivaceus*, and one of the latter, *T. centimetralis*. The differences in external morphology and in the internal organs are clearly presented in a table and their geographical distribution in the various States of Brazil is given. There are useful hints regarding the technique of collection of the molluscs, their preservation and feeding in the laboratory, the mode of search for cercariae and collection of these for inoculation, the details of inoculation of animals and the experimental infection of the snails. All these details are clearly set out and described in the text and illustrated in 8 figures. Those interested should consult the original where minute directions are given in plain and simple language.

H. Harold Scott

MOORE, D. V. & MELENEY, H. E. **Adaptability of *Schistosoma mansoni* of Human Origin to Mice and Hamsters.** *Exper. Parasit.* New York. 1952, Mar., v. 1, No. 2, 157-60.

STUNKARD [this *Bulletin*, 1947, v. 44, 432] reported that it was the general belief that man and monkeys are the only definitive hosts of *Schistosoma mansoni* capable of passing eggs of this fluke in their faeces, although other animals can be infected with this species.

The present authors infected mice with cercariae obtained from the snail *Australorbis glabratus* (itself infected by miracidia derived from eggs passed by a human patient) and found that the infected mice regularly passed eggs in their faeces. They therefore studied further the transmission of *S. mansoni* to small laboratory animals.

Eggs of *S. mansoni* were obtained from 10 Porto Rican patients, and *A. glabratus*, either wild or reared in the laboratory, were infected with miracidia artificially hatched from the eggs, each snail being exposed to 5 or 10 cercariae. The cercariae were used to infect mice and golden hamsters. Examination of the faeces of the mice and hamsters began 5 weeks after their infection and went on each half-week until viable eggs were found by the sedimentation-hatching technique of FAUST and MELENEY [*Ibid.*, 1925, v. 22, 468], which was also used to obtain eggs from the human stools.

Ten snails were each exposed to cercariae from each of the 10 patients from whose stools the eggs were obtained, except that 6 snails only were exposed to the eggs from one patient. The snails shed cercariae 20 to 39 days after exposure to the miracidia and the infection-rate of the snails was 30 to 100 per cent. Ten to 13 mice were each exposed to 100 to 200 cercariae from each group of snails representing each patient. The number of mice used was 111 and all of them passed viable eggs of *S. mansoni* in their faeces, the eggs appearing 6 to 7½ weeks after exposure to infection. Each of 5 golden hamsters was exposed to 400 cercariae derived from snails infected from only one of the human patients who provided the eggs. They all passed viable eggs in their faeces 6½ weeks after exposure to infection. Moore and Meleney (in the press) have also found that the rice rat, which will enter water in search of food, can act as a definitive host of *S. mansoni* and can pass eggs in its faeces. The authors conclude that the gradual adaptation of mice and hamsters to human strains of *S. mansoni* is not necessary. *S. mansoni* adapts itself to new molluscan intermediate hosts in new areas, but does so only with difficulty. It appears to be also restricted to a few definitive hosts, because man and monkeys (and the rice rat) are the only definitive hosts so far found to be naturally infected. *S. japonicum*, however, can use a variety of definitive hosts and the work recorded above suggests that it is possible that rodents, and possibly other mammals, may be naturally-infected definitive hosts of *S. mansoni*.

G. Lapage

GOHAR, M. A., EISSA, A. A. & SEBAL, I. **Antibody Response in Egyptian Splenomegaly.** *Amer. J. Trop. Med.* 1951, Sept., v. 31, No. 5, 605-10, 4 figs.

The agglutinin antibody response to 2 injections (a week apart) of *Salm. typhi* suspensions was measured over a period of 40 days in (a) 3 normal persons, (b) 3 patients suffering from Egyptian splenomegaly, (c) 2 patients with splenomegaly in whom the spleen was removed 6-12 days respectively after the last dose of organisms, and (d) 7 patients to whom the organisms were given 16 days to a month after splenectomy.

Compared with the first group the responses of groups (b) and (c) were poor. In the fourth group the response in those splenectomized 16 days before injection was poor, but approached normal in those splenectomized a month beforehand.

The authors suggest that the splenic poverty in reticulo-endothelial cells accounted for the poor results. The improvement in group (d) might be explained by "compensatory hypertrophy of healthy lymphoid tissue".

[The argument is based on very meagre evidence. No clear criteria of diagnosis of "Egyptian splenomegaly" are given in the cases quoted.]

B. G. Macgrath

HARRIS, F. C. **A Field Trial of Miracil D for the Mass Treatment of Bilharzia in the Gold Coast.** *West African Med. J.* 1952, Apr.-May-June, v. 1 (n.s.), No. 2, 56-8.

"A clinical trial of Nilodin was carried out on 143 Gold Coast school boys. Of 79 boys given a total dosage of 75 mg. per kg. of body weight only 34 (43 per cent.) ceased to pass live schistosome eggs. A further attempt was made on another group of boys, giving them a total dosage of 100 mg. per kg. and 125 mg. per kg., but this had to be abandoned.

"From this small-scale experiment it would appear that Nilodin is insufficient in a total dosage of 75 mg. per kg. of body weight, and higher doses are not tolerated. The difficulties of mass treatment with Nilodin in this region have been indicated."

BARTON, W. L. **The Treatment of Urinary Bilharzia.** *East African Med. J.* 1952, Feb., v. 29, No. 2, 41-4.

Of 1,270 patients admitted to Kilifi Hospital [Coast province], Kenya, 23 per cent. were found to be suffering from urinary schistosomiasis; 314 of these sufferers were treated intensively for 2 days with sodium antimony tartrate. After some initial troubles, due to faulty technique, toxic side-effects of the treatment fell and the percentage of apparent cures increased; the final figures were 10 per cent. and 62 per cent. respectively. In the whole series of 314, two patients died of heart-block; the total mortality was 0.6 per cent. These fatalities were attributable to failure to carry out instructions, for the patients who died refused to remain at rest during the treatment, as they had been told to do.

The intensive sodium antimony tartrate treatment was well received by the patients; the results were encouraging; and the low fatality rate it causes does not contra-indicate its continued employment.

A. R. D. Adams

HSÜ, H. F., LI, S. Y., WANG, C. K., FAN, P. C. & HUANG, T. C. **Studies on Schistosomiasis japonica in Formosa.** *Amer. J. Trop. Med. & Hyg.* 1952, Mar., v. 1, No. 2, 287-301, 6 figs. [19 refs.]

It is well recognized that schistosomiasis due to *S. japonicum* occurs in Formosa and that the intermediate host is *Oncomelania formosana*, but



considerable doubt exists regarding the endemic areas of the disease and the distribution of the snail host. The authors begin their paper by reviewing the Japanese literature concerning the epidemiology of schistosomiasis in Formosa, and from this study they conclude that the main centre of the disease is at Changhua Hsien, one of the most important rice-growing centres of Formosa, in the mid-Western portion of the Island. Dr. Hsü and his colleagues had intended to commence their investigation by examining the human population in this area, but circumstances compelled them to abandon this plan, and instead they have studied the distribution, habits and infection rate of the local molluscan host.

In the Changhua Hsien area 628 villages were surveyed, and *Oncomelania formosana* snails were found in 140 of them. The infected villages tended to occur in the central portion of the county, and extended over an area of some 273 sq. km. The snails were usually found in small irrigation ditches, especially if these were shaded, and they tended to be absent from ditches of more than two metres in width. It was also noted that *O. formosana*, unlike several other species of *Oncomelania*, thrives in water turbid with fine suspensions of silt and clay particles. In order to add to their knowledge of the epidemiology of schistosomiasis in the area the authors dissected up to 300 snails from one ditch in every village where the presence of *O. formosana* had been recorded. Owing, however, to the paucity of the snail population in some villages, the intended number of 300 snails was not always reached. Altogether 38,241 snails from 140 ditches in 140 positive villages were examined. "On the average, 1.3 per cent. [of the snails] were positive, and in the infected ditches the range of infection was from 0.3 to 30 per cent, with its mean at 2.4 per cent, median at 1.2 per cent, and mode at 0.3 per cent. The frequency curve of the percentage of infection, if plotted, will be a curve of positive skewness." The authors state that "The examination of *Oncomelania* snails for cercariae was done by crushing living snails between two slides, three snails being crushed at the same time. One drop of water was added to a crushed specimen and the latter was teased and examined under a binocular dissecting microscope. Finding of sporocysts alone was also regarded as a positive infection." [It would appear from this description that some of the "positive snails" may have been infected with cercariae other than those of *S. japonicum*.]

R. M. Gordon

HUNTER, G. W., KAUFMAN, E. H., JR. & PAN, C. **Studies on Schistosomiasis.**

**III. Copper Oleate Ointment in Protection Experiments against *Schistosoma japonicum*.** *Exper. Parasit.* New York. 1952, Mar., v. 1, No. 2, 168-75. [12 refs.]

The authors have investigated the use of copper oleate ointment as a protection against penetration of the skin of mouse and man by cercariae of *Schistosoma japonicum*. Copper oleate is a dark blue viscous substance, at body temperature insoluble in water and alcohol but soluble in fat solvents like ether, and is more stable in alkaline or neutral solution than in acid. It is best spread on the skin by using a 20 per cent. solution in ether and allowing the solvent to evaporate, when a tenacious film is formed which can be removed by the original solvent. The cercariae used was obtained from the surface film after crushing of infected snails in aerated tap water. Mice 6 to 8 weeks old were shaved extensively 24 to 48 hours before being lightly anaesthetized and immobilized and brought into contact with 100 cercariae maintained in water in a shallow vessel for a period of 30 minutes. Copper oleate 20 per cent. in

ether was applied when desired to the shaved area and was allowed to dry for one hour before exposure of the mice and was wiped off 2 to 24 hours later.

Exactly the same procedure was followed with control mice in the absence of copper oleate. The exposed animals were sacrificed after 3 to 8 weeks and examined for schistosomes, with the use of a perfusion technique described by the authors [this *Bulletin*, 1951, v. 48, 1012] while sections of liver and spleen were also made. By the use of copper oleate, 38 mice were completely protected when exposed as described above, or at intervals over a period of 48 hours, whereas nearly 80 per cent. of 39 control mice became infected. Experiment indicated that protection by copper oleate was not a mechanical effect but that contact with it was necessary to kill cercariae. It did not appear to be toxic for the mice. It is also stated that 95.5 per cent. of workers in paddy fields were protected against infection by copper oleate for a period of 8 hours, but details are reserved for future publication.

J. D. Fulton

MELENEY, H. E., MOORE, D. V., MOST, H. & CARNEY, B. H. **The Histopathology of Experimental Schistosomiasis. 1. The Hepatic Lesions in Mice Infected with *S. mansoni*, *S. japonicum* and *S. haematobium*.** *Amer. J. Trop. Med. & Hyg.* 1952, Mar., v. 1, No. 2, 263-85, 11 figs. on 6 pls.

The material studied consisted of sections of the livers of 15 uninfected mice and 313 mice infected with schistosomes of various species, the number of mice thus examined and the nature of the infections being as follows: 15 uninfected mice; 104 unisexual male infections with *S. mansoni*; 71 unisexual female infections with *S. mansoni*; 66 bisexual infections with *S. mansoni*; 29 unisexual male infections with *S. japonicum*; 22 unisexual female infections with *S. japonicum*; 4 bisexual infections with *S. japonicum* and 17 unisexual male infections with *S. haematobium*.

The results obtained from examining the normal mice livers were interesting and emphasized the importance of control observations. Since they have a bearing on the authors' conclusions they are quoted here in full: "Uninfected mice. In young mature mice the liver may show practically no cellular infiltrations either in the periportal connective tissue or in the parenchyma, but more often it contains small accumulations of mononuclear cells about the portal venules and occasionally larger circumscribed nodular accumulations extending into the liver parenchyma. It may also contain small circumscribed accumulations of mononuclear and polymorphonuclear cells in the parenchyma, apparently not associated with portal venules. In old mice there is usually more cellular infiltration, and in two of our mice, each about a year old, there was in addition an area in the parenchyma of intense polymorphonuclear infiltration with loss of liver cells and fragmentation of the invading cells." In this connexion it should be noted that LEE [*Comptes Rendus, Congrès International de Médecine Tropicale et d'Hygiène*, 1932, v. 4, 373-386] recorded, in 1932, the occurrence of lymphocytic infiltrations in periportal spaces and occasionally between columns of liver cells in 24 out of 25 Chinese hamsters infected with cercariae of *S. japonicum*, but he discounted these findings because he discovered similar infiltrations in uninfected animals. [The original paper by Lee refers to "unisexually infected hamsters".]

The results of comparing histological appearances of liver tissue from animals with bisexual infections, and with eggs in the tissues, with livers from animals with unisexual infections and, therefore, with no eggs in the tissues, have convinced the authors of the present paper that pathological lesions in the liver may be produced independently of egg production. They are very cautious regarding the cause of these lesions, but express the view that they

are probably caused by a toxic product of the worms, and that the absence of fibrosis in the unisexual infections suggests that, in mice at any rate, it is necessary for both sexes of the worms to be present in order to produce cirrhosis of the liver.

The authors' summary and conclusions are as follows :—

" 1. Histological sections of livers from white mice infected with male or female *Schistosoma mansoni*, *S. japonicum* or *S. haematobium*, and with both sexes of *S. mansoni* or *S. japonicum* prior to egg deposition, were examined to study lesions associated with the presence of worms in the portal-mesenteric vessels in the absence of lesions produced by eggs. Most of this material came from *S. mansoni* infections.

" 2. In unisexual *S. mansoni* infections periportal infiltration of mononuclear and polymorphonuclear leucocytes appeared after 3 to 4 weeks in the majority of unisexual infections and increased in intensity in infections up to about 12 weeks in duration, after which it tended to become less intense and was predominantly mononuclear.

" 3. Cellular infiltration in the parenchyma of the liver, predominantly polymorphonuclear, occurred in some animals, apparently independent of extensions from the periportal infiltrations. These increased in frequency and intensity in infections up to about 12 weeks in duration, but were rare in infections 20 weeks or more in duration.

" 4. Areas of coagulative necrosis in the parenchyma of the liver were found in a considerable number of animals. They became invaded by polymorphonuclear leucocytes with later disappearance of liver cells and invasion of mononuclear and multinuclear cells. Worms were sometimes present in venules immediately adjacent to these lesions, giving the impression that they may have been infarcts initiated by temporary obstruction of the blood supply by the worms.

" 5. No evidence of development of cirrhosis of the liver was found in unisexual infections up to 95 weeks in duration.

" 6. Some of the unisexual infections with *S. japonicum* or *S. haematobium* showed the same types of lesions as those infected with *S. mansoni*. In general the lesions were less intense, but accurate comparison is not warranted.

" 7. In bisexual *S. mansoni* infections up to 5 weeks in duration periportal and parenchymal cellular infiltration and coagulative necrosis appeared earlier and were more frequent and intense than in unisexual infections of the same duration. Occasional mural thrombi were found in portal venules.

" 8. Some uninfected mice had mild degrees of periportal and parenchymal cellular infiltration, but areas of coagulative necrosis were not seen.

" 9. Although some infected mice failed to show any lesions in the liver, it seems possible that the intense cellular infiltrations and areas of necrosis were causally related to the presence of worms in the mesenteric-portal blood vessels."

This is an important paper which does not lend itself to further summarization and should be consulted in the original by those interested.

R. M. Gordon

RITCHIE, L. S., HUNTER, G. W., KAUFMAN, E. H., Jr., PAN, C., NAGANO, K., YOKOGAWA, M. & SZEWCZAK, J. T., with the technical assistance of Y. HISHINUMA, M. SHIMIZU & S. ASAKURA. **Parasitological Studies in the Far East. V. An Epidemiologic Survey in Okayama Prefecture, Honshu, Japan.** *Japanese Med. J.* 1951, Oct., v. 4, No. 5, 307-14. [13 refs.]

" A total of 1260 individuals of three communities in Okayama Prefecture, Honshu, Japan, were examined for intestinal parasites. Of this number, 89.4% were parasitized ; 85.6% with helminths and 38.2% with protozoa.



"*Clonorchis sinensis*, known to be highly endemic in Okayama occurred with an incidence of 40.3% at Kojo, but only 6.4% at Okayama City and 3.9% at Notani."

MACKIE, A. & RAEBURN, J. **The Effect of some Oxidation Products of Phenothiazine on Liver Fluke (*Fasciola hepatica*) in Vitro.** *Brit. J. Pharmacol. & Chemotherapy*. 1952, June, v. 7, No. 2, 215-18, 4 figs. [13 refs.]

"1. Phenothiazone, thionol, and phenothiazine sulphoxide, oxidation products of phenothiazine, have been prepared and tested at various concentrations against liver fluke (*Fasciola hepatica*) in vitro.

"2. Phenothiazone had a lethal effect at a concentration of 1:8,000 and was paralyzant at 1:16,000. Thionol and phenothiazine sulphoxide had only paralyzant effects at 1:1,000 and 1:4,000 respectively."

MACKIE, A. & RAEBURN, J. **The Influence of Groups in the Molecule of 2:3-Dihydro-3-Ketobenzo-1:4-Thiazine on its Effect on Liver Fluke (*Fasciola hepatica*) in Vitro.** *Brit. J. Pharmacol. & Chemotherapy*. 1952, June, v. 7, No. 2, 219-22, 1 fig.

"1. 2:3-Dihydro-3-ketobenzo-1:4-thiazine and derivatives with substituents in the 6- and 6:7-positions were tested against liver fluke (*Fasciola hepatica*) in vitro and the effects recorded kymographically.

"2. All the compounds, which could be tested over a wide range of concentrations, showed paralyzant effects.

"3. Minimum effective concentrations (MEC) were estimated and it was possible to arrange the substituent groups in the following order of potency (MEC in parentheses): Cl(1:8,000) > N<sub>3</sub>, NO(1:6,000) > I(1:5,000) > NO<sub>2</sub>, 6:7-dimethoxy (1:4,000) > NH<sub>2</sub>HCl(1:3,000) > unsubstituted compound, F(1:2,000) > NH<sub>2</sub>, CH<sub>3</sub>.CO.NH, CNS, SH, 6:7-dihydroxy (1:1,000).

"4. The 6-amino- and 6-mercapto-derivatives were paralyzant at a concentration of 1:1,000, and severely reduced the subsequent response to amphetamine sulphate.

"5. Owing to the insolubility of the 6-arsonic acid, 6-stibonic acid, 6-chloromercuri-derivatives and bis-(2:3-dihydro-3-ketobenzo-1:4-thiazin-6-yl), no minimum effective concentration could be obtained, but a 1:4,000 suspension of the 6-chloromercuri-derivative produced almost complete paralysis; the 6-arsonic acid was slightly depressant and the other two derivatives without effect at this concentration."

SIGUIER, F., FELD, PIETTE, M., WELTI, J. J. & LUMBROSO, P. Tribulations neurologiques d'un jeune berger atteint de distomatose cérébrale à "*Dicrocoelium lanceolatum*". [**Neurological Troubles of a Young Shepherd Suffering from Cerebral Infection with *Dicrocoelium lanceolatum* (= *D. dendriticum*)**] *Bull. et Mém. Soc. Méd. Hôpit. de Paris*. 1952, Nos. 9/10, 353-9, 6 figs.

Cerebral "distomatosis" is very rare. The authors describe one case which they interpret as being a case of infection of the brain with the lesser liver fluke, *Dicrocoelium dendriticum* (= *D. lanceolatum*). The patient was 17 years old. In November, 1950, he developed convulsive crises and Jacksonian gait, affecting the left-hand side, with slight symptoms of deficiency in that side. Several days later, when these crises were repeated, he had a hemiplegia on the right-hand side with aphasia. Finally a meningeal syndrome was imposed

on these symptoms. A positive tuberculin skin test suggested tuberculous meningitis and this seemed to be confirmed by the finding of 40 lymphocytes per cmm. by lumbar puncture; but nothing else supported this diagnosis. Investigation of the brain by arteriography and ventriculography revealed no abnormalities. The electroencephalogram showed slow, irregular waves superimposed on the alpha. There was, however, an eosinophilia of 48 per cent., which was maintained at levels of 58 and 50 per cent. The patient was a shepherd and his father was a master-shepherd in charge of 700 animals and the patient remembered having eaten, on several occasions, cress from the pastures of his father's animals. The authors decided that the infection probably came from this cress. The patient's intradermal reaction to "Distoma" antigen was positive and eggs of *D. dendriticum*, illustrated in fig. 6, were found in his faeces.

In the literature the authors found no references to cerebral infection with *Dicrocoelium* in man, but they did find references [not quoted] to the transmission of *D. dendriticum* or its eggs by the blood to the brain [presumably of animals that are normal hosts of this fluke] in which it caused the formation of cystic cavities responsible for various neurological symptoms. Cerebral infection with *Fasciola hepatica* is rarer still, but LAVIER [no ref.] has described one case. The authors found records of less than 100 cases of human infection with *Dicrocoelium*, most of which were infections of the liver described by Russian, Rumanian or Swiss authors and they were diagnosed by examination of the faeces, a method which is not adequate, because eggs of this fluke may be derived from the eating of food infected with them. ZOTA and KALAUTARIAN [no ref.], however, found adult and living *Dicrocoelium* in the livers of two human patients. Clinical accounts of the infection are very scarce and most of them describe digestive troubles; but some [referred to by the author without references] describe grave anaemia, enlargement of the liver and abdominal pain, but none of them mention neurological symptoms. [The treatment and subsequent history of the patient described are not considered in this paper.]

G. LaPage

HOOD, M. **Laboratory Diagnosis of Platyhelminthiasis.** *Amer. J. Clin. Path.* 1952, Apr., v. 22, No. 4, 396-402. [21 refs.]

CHANG, H. F. **Areca Nut in the Treatment of *Diphyllbothrium latum*.** *Peking Nat. Hist. Bull.* 1950-51, Dec.-Mar., v. 19, Pts. 2/3, 273-5.

Areca nut has been found to be effective in the treatment of three tapeworms, *Taenia solium*, *Taenia saginata*, and *Hymenolepis nana*. It is also effective against *Fasciolopsis buski*. The author reports his experiences in the treatment of *Diphyllbothrium latum* infection in one case.

The patient was a male, aged 24 years, a native of the U.S.S.R., who had recently arrived in China. He complained of low fever, a cough with sputum, irregular abdominal pain in the left lower quadrant, of 2 months' duration, and occasional looseness of the bowels but no blood or mucus. He was admitted as a suspected case of pulmonary tuberculosis.

Clinical and X-ray examinations showed nothing abnormal. The blood examinations were within normal limits except that the erythrocyte sedimentation rate was 20 mm. in one hour: no eosinophiles were found. The sputum examination was negative. The faeces showed numerous eggs of *D. latum*.

A decoction of areca nut, 200 ml. from 100 gm. of areca nut, was given in the early morning before any food was taken. On the previous night after a light meal, 50 ml. of 50 per cent. magnesium sulphate had been given. Two

hours after administration the patient passed a loose motion containing a mass of worms and half-an-hour later another similar stool. Four tapeworms were found with the heads attached.

No ova were found in the stools subsequently and the abdominal pain did not recur. [See also this *Bulletin*, 1952, v. 49, 161.] *L. E. Napier*

BEAVER, P. C. & SODEMAN, W. A. **Treatment of *Hymenolepis nana* (Dwarf Tapeworm) Infection with Quinaerine Hydrochloride (Atebrin).** *J. Trop. Med. & Hyg.* 1952, May, v. 55, No. 5, 97-9.

The authors refer to previous work on the treatment of *H. nana* infections with atebrin [mepacrine] and state that the results generally have been disappointing [this *Bulletin*, 1946, v. 43, 939; 1951, v. 48, 1134; 1952, v. 49, 419]. They now report the results of treatment in 8 boys, aged 6-19, who received 0.6 to 0.8 gm. of quinaerine hydrochloride in a single dose on an empty stomach, followed one hour later by a saline purgative. Worm loads were estimated on the basis of numbers passed and egg-counts were made at 1- to 3-week intervals before treatment and flotation tests were carried out at 1-2-week intervals afterwards, for 9 weeks. In 7 cases, stool examinations with egg-counts were made after a year.

Three patients were consistently negative up to 9 weeks: the other 5 apparently passed a high percentage of worms. In one case, where the pre-treatment egg-count averaged 78.3/mgm., some 6,000 worms were recovered. It seems that *H. nana* produces relatively few eggs. The results were poor from the point of view of cure, but the worm load was considerably reduced in those who remained positive. After 1 year, infections were found in only 3 of 7 patients and the highest count was 3 eggs/mgm. of faeces.

Unfortunately estimation of clinical improvement was not made, as the patients were inmates of an institution for mental defectives, whose clinical histories could not be relied upon, but the authors conclude that "Atebrin is highly effective in the removal of this parasite, although single doses frequently fail to eradicate the infection". *H. J. O'D. Burke-Gaffney*

SAIZ MORENO, L. La hidatidosis como problema sanitario. [Hydatid Disease as a Public Health Problem] *Rev. Sanidad e Hig. Pública.* Madrid. 1951, Sept., v. 25, No. 9, 499-529, 11 figs.

MIYAZAKI, I. *Raillietina madagascariensis* found in Kyushu, Japan. *Kyushu Mem. Med. Sci.* Fukuoka. 1950, June, v. 1, No. 1, 1-6, 12 figs. on 2 pls. [10 refs.]

"1. *Raillietina madagascariensis* (Davaine, 1869) was found in rats in Kagoshima City, Kyushu. This is the first record of the parasite in Japan.

"2. Among 269 *Rattus norvegicus*, 26 (9.7%) were naturally infected with the parasite, its number per host being 1 to 67 (average 12.3).

"3. Among 31 *Rattus rattus*, only 1 (3.2%) harboured 7 parasites."

GREINER, H. Ueber eine medizinale Vergiftung mit Extractum filicis maris aethereum. [Poisoning by Ether Extract of *Filix mas*] *Med. Klin.* 1952, May 9, v. 47, No. 19, 645-7. [16 refs.]

Preparations made from the Male Fern (*Aspidium filix mas*) have been used for the treatment of tapeworm infestation for about 2,000 years. Records from



the Middle Ages show that these preparations were then known to give rise to toxic effects in some instances. A considerable number of poisonings have now been reported, the doses in these cases having ranged from 4.5 to 34.0 gm. of the extract, a variation no doubt partly the result of differences in the amount of the unknown active substance in different samples of the fern.

The symptoms of poisoning consist in an initial nausea, vomiting and diarrhoea followed after some hours by signs and symptoms referable to the central nervous system. There may be giddiness, headache, disturbances of consciousness and disorder of the respiratory and circulation centres. Psychoses have been observed. The eyes may be affected by loss of accommodation—there may be haemorrhages and also optic atrophy.

The greatest care should be taken in giving the drug to persons who have kidney, liver or heart disease.

An account is given of a man of 47 years of age who, stated to have had several courses of treatment for tapeworm in 12 months, was again treated in hospital with a male fern preparation. He did not feel well when the treatment had been given but was discharged and died suddenly 17 days later.

The post-mortem findings, which were mainly those of congestion of kidneys, liver, pancreas and brain, are described.

M. E. Delafield

BEAVER, P. C. **The Detection and Identification of some Common Nematode Parasites of Man.** *Amer. J. Clin. Path.* 1952, May, v. 22, No. 5, 481-94, 26 figs. [23 refs.]

This paper contains a great deal of detailed practical information and requires to be read in the original if its full value is to be appreciated.

The author gives much useful information on the recovery of worms from stools and the recognition of the adult stages of the commoner nematodes infecting man. Methods of finding nematode eggs and larvae in faeces are described step by step, with useful "tips" and comments on technique. The last feature includes a list of causes of poor results sometimes obtained in the use of zinc flotation methods: particularly useful is the table showing the results obtained by students, compared with those of trained instructors, in the examination of 2,681 stools from children. The percentage of false negative results found by the students varied from 9.7 in the case of *Ascaris* to 53.0 in the case of *Endolimax*.

A short note is given on perianal sampling and this is followed by descriptions of differential characters of eggs and larvae. A brief final section discusses the larval stages of nematodes in tissues and the difficulty of identifying them. The paper is illustrated by several clear line-drawings of nematode adults, larvae and eggs. All whose work involves the routine detection of nematode parasites will profit from this essentially practical and informative paper.

H. J. O'D. Burke-Gaffney

KAGIOKA, T., MIKI, T. & YOSHIDA, S. [Some Notes on the Ascariasis Diagnosis by means of the Granules in the Soft Palate Region] *J. Osaka City Med. Center.* 1951, Oct., v. 1, No. 1, 56-9. [In Japanese.] [English summary.]

The authors noticed colourless granules in the uvulae of patients suffering from ascariasis. The granules were small, non-inflammatory and varied from "a few" to "scores" in number. They are thought to be swollen orifices of mucous glands.

In 1,015 schoolchildren, 80 per cent. showing these granules had *Ascaris* ova in the stools, while only 20 per cent. of children without granules were so infected. Granules were found in 92-95 per cent. of infected persons.

In 81 adults aged 17-58, *Ascaris* infection was found in 86 per cent. of those with granules, but in 111 persons between 61 and 87, granules were rare; even in those infected, granules occurred in only 25 per cent.

The granules tended to disappear with the infestation. In 21 of 61 recovered cases they disappeared within 10 days of treatment and in the remainder they diminished. It is noted that 14 of 64 persons with uvular granules, but with no eggs in the stools, passed the worms after treatment.

H. J. O'D. Burke-Gaffney

KERR, K. B. & CAVETT, J. W. **A Technic for Initial Evaluation of Potential Anthelmintics.** *Exper. Parasit.* New York. 1952, Mar., v. 1, No. 2, 161-7, 1 fig.

A simple and rapid *in vitro* screening method for anthelmintics is described, with the use of *Ascaridia galli*, the large intestinal round worm of chickens, as the test object. The technique, in which whole worms of length 3 to 4 inches are used, is based on the nerve-muscle technique of BALDWIN [this *Bulletin*, 1944, v. 41, 54; 1948, v. 45, 921] who used the anterior portion of *A. lumbricoides* for the same purpose. Worms removed from the chicken could be kept in a bath around 40°C. in 1 per cent. saline for 24 hours if several changes of the bathing fluid were made. During the experiment one end of the worm was attached by thread to a glass hook at the bottom of a constant-temperature bath maintained at 37° to 40°C., without damage to the cuticle. The other end was attached to a light heart lever with aluminium wire stylus. The movements of the worm were recorded on a smoked drum. Normal activity in the absence of drug was recorded for 5 minutes or more before the substance in solution to be tested was used to replace the saline, and definite responses were elicited in 10 to 15 minutes. A fresh worm was used for each test, which was repeated till consistent results were obtained. The effect of nicotine was first studied and definite effects were obtained with a 2 mgm. per cent. solution. A paralysing effect was caused, followed by contraction of the worm and then a gradual relaxation. Atropine also caused paralysis accompanied by relaxation. This "atropine effect" was paralleled by phenothiazine. The effect of a number of recognized anthelmintics and other substances is recorded in a table. Many of the established anthelmintics produced the "nicotine effect" and there appears to be a correlation between this effect and anthelmintic activity under the conditions of test and the correlation may extend to other intestinal nematodes.

J. D. Fulton

McFADZEAN, J. A. **Investigations into the Cause of Microfilarial Periodicity.** *Brit. Med. J.* 1952, May 24, 1106-9, 4 figs. [16 refs.]

HAWKING and THURSTON (*Trans. Roy. Soc. Trop. Med. & Hyg.*, 1951, Dec., v. 45, No. 3, 307-28) described an experimental filarial infection in African monkeys, which exhibited microfilarial periodicity closely similar to that of *W. bancrofti*; by its study, they showed that when microfilariae disappeared from the blood during the day time, it was because they had accumulated in the small vessels of the lungs. The present paper carried the investigation a stage further by studying some of the stimuli which cause the microfilariae to migrate backwards and forwards between these two sites. During the day time (when microfilariae are practically absent from the blood) exposure of the monkeys to oxygen concentrations of 60 per cent. caused a pronounced migration from lungs to blood. A similar result was produced by lowering the oxygen concentration to 10 per cent. On the other hand raising the alveolar concentration of carbon dioxide (by blowing carbon dioxide against the monkey's nose) or lowering it (by hyperventilation) caused no significant change in the microfilarial count. When the same experiments were performed at night

(when the blood contains many microfilariae) exposure to carbon dioxide had no effect whereas exposure to increased oxygen, or production of anoxia, *increased* the microfilarial count as in the day time. The literature shows that there is a 24-hour cycle in the excretion of phosphates which resembles the cycle of nocturnally periodic microfilariae. However, intravenous injection of phosphate did not affect the microfilarial count, and during the rise of the count following exposure to increased oxygen there was no change in the inorganic phosphorus of the plasma. Accordingly it was concluded that there is no direct relation between the phosphate cycle and the microfilarial cycle. The microfilarial count was not affected by general vasodilation induced by hexamethonium iodide, or by changes in the temperature, pulse rate, or respiratory rate. However, migration of microfilariae from lungs to blood was promoted by energetic exercise. It is not yet possible to use these experimental findings to explain the causation of the microfilarial cycle.

F. Hawking

DEANE, L. M. Observações sobre alguns hábitos dos adultos de *Culex fatigans*, o principal transmissor da filariose em Belém, Pará. [**Notes on Some Habits of the Adults of *Culex fatigans*, Principal Vector of Filariasis in Belém, Brazil**] *Rev. Serviço Especial de Saúde Pública*. Rio de Janeiro. 1951, Apr., v. 4, No. 2, 423-64, 6 graphs & 1 plan. English summary.

This paper gives the facts and figures obtained during a mosquito survey conducted between April 1948 and June 1949 in two adjacent districts in Belem, Brazil, where *Culex fatigans* is the main vector of *Wuchereria bancrofti*. The work was particularly directed towards investigating the habits of the vector mosquito and an analysis of the data shows that *C. fatigans* is far more domestic than any of the other 20 local species. For instance, of 2,270 female *C. fatigans* obtained, 2,222 were caught in houses, and among all the species, some 99 per cent. of the females caught in houses were *C. fatigans*. Precipitin tests were made on the stomach contents of the female mosquitoes and showed that this species had a definite preference for human blood. Weekly half-hour captures in 20 houses showed that *C. fatigans* occurred all the year round with a peak of prevalence in March coinciding with the height of the wet season. Other figures showed that *C. fatigans* females became increasingly abundant in houses after twilight and reached a maximum density about the middle of the night. Though about half the mosquitoes obtained were caught in the bedrooms, all rooms in all parts of the houses were frequented to some extent, and specimens were caught, not only on the lower parts of the walls, but on the upper portions also and behind and under furniture.

These observations, all supported by the data, indicate that for the control of *C. fatigans* the indoor spraying of residual insecticides is justified. The high density throughout the 12 months means that more than one spraying is necessary in the course of a year. Finally, the spraying must not be restricted to the lower parts of the walls of the bedrooms but must include the whole of the wall surface in all the rooms as well as under and behind the furniture.

The paper is illustrated by a map and numerous tables and charts.

H. S. Leeson

VU-CONG-HOE. Contribution à l'étude anatomopathologique des lésions filariennes de l'appareil uro-génital en Indochine. [**Anatomical and Pathological Studies of Filarial Lesions of the Genito-Urinary System in Indo-China**] *Méd. Trop.* Marseilles. 1951, Nov.-Dec., v. 11, No. 6, 915-20. [17 refs.]

In discussing the pathological changes of filariasis in Indo-China the author does not concern himself with the species, whether *Wuchereria bancrofti* or



*W. malayi*. As is well understood, the adult filaria lives for several years in the lymphatic vessels and after death it degenerates, becoming transformed into fibrous tissue or calcified. These changes are seen when this parasite attacks the genito-urinary system.

Philip Manson-Bahr

HUARD, P., VU-CONG-HOE & TRAN-ANH. Un cas d'hématochylurie filarienne suivie de nécropsie. [**A Case of Filarial Haematochyluria, with Autopsy Findings**] *Méd. Trop.* Marseilles. 1951, Nov.-Dec., v. 11, No. 6, 911-14, 1 fig.

This paper is of considerable interest as it contains an account of the autopsy findings in a case of haematochyluria in a patient in Hanoi. A pyelogram taken during the last illness demonstrated some communication of the chyloferous vessels with the renal pelvis. This finding was reinforced by a retrograde pyelogram which showed a column of dilated lymphatics clustered round the right ureter and extending to the renal pelvis. [A diagram attached to the pyelogram figure makes this clear.] Microfilariae were seen in the urine intermittently, but disappeared eventually after Notezine treatment.

In the genito-urinary system there were revealed large lymphatic varices extending bilaterally from the epididymis to the abdominal lymphatic glands. A collection of tangled lymphatic vessels filled the sacral cavity forming a plexus joining the pelvic lymphatics to those of the peri-aortic group. These vessels were hypertrophied as well as those of the kidneys.

The thoracic duct was dilated and running parallel to it there were numerous retro-aortic lymphatics.

An anatomo-pathological examination of the kidney and testes revealed no portion of adult filariae of microfilariae.

In the kidney itself there were severe nephritic changes, with oedema of the glomeruli and dilatation of the urinary tubules.

The lymphatic vessels themselves were dilated externally and thrombosed with lymph clot internally. These findings are important because of the rarity of published reports on filarial haematochyluria and on the grounds that this condition is reputed to be benign which, as this case demonstrates, is not always true.

Philip Manson-Bahr

PATEL, J. C. Chyluria. A Report of Two Cases treated with Sodium Pentavalent Antimony Glueconate. *Indian J. Med. Sci.* 1952, May, v. 6, No. 5, 318-20.

DEJOU, L. Guérison d'un oedème chronique éléphantiasique du membre inférieur par le débridement de l'anneau crural. [**Cure of Chronic Oedematous Elephantiasis of the Lower Limb by Debridement of the Crural Ring**] *Bull. Soc. Path. Exot.* 1952, v. 45, No. 2, 217-21.

KERSHAW, W. E. Studies on the Epidemiology of Filariasis in West Africa, with special reference to the British Cameroons and the Niger Delta. II.—The Influence of Town and Village Evolution and Development on the Incidence of Infections with *Loa loa* and *Acanthocheilonema perstans*. *Ann. Trop. Med. & Parasit.* 1951, Dec., v. 45, Nos. 3/4, 261-83, 8 text figs., 1 map & 6 figs. on 2 pls. [12 refs.]

Three evolutionary stages, those of radiation, adaptation and fine adjustment, are discussed in relation to the development of parasitism. It is suggested that a parasitic system involving separate complicated life-cycles in various hosts, vertebrate and invertebrate, should be considered as evolving as an integrated whole, and that the ultimate fortunes of the parasite are dependen

upon unknown potentialities of adaptability both of the hosts and of the parasite. Any change in the environment of the associated hosts may possibly result in stabilization of the parasite at a new level of incidence, either higher or lower, or in extinction, or in a completely new evolutionary venture.

The normal incidence of infections with *Loa loa* and *Acanthocheilonema perstans* in villages in the undisturbed rain-forest of the British Cameroons is discussed and contrasted with the incidence of filariasis in an artificial village on a rubber estate at Sapele in Southern Nigeria, and with that occurring in Kumba, a developing market-town in the British Cameroons.

The author shows that the different environments in these three localities have produced and sustained alterations in the level on which infections with *L. loa* are maintained.

"In the rubber estate village, the higher incidence of infections with *L. loa* among the men and the lower incidence among the women, as compared with their counterparts in a village in the rain-forest, are due to the selective difference in exposure to the bites of infected *Chrysops*. The rubber-tappers are involved in a combination of circumstances, all of which are so altered as to increase the probability of transfer at each state of the life-cycle of the parasite—a combination which constitutes, in fact, an artificial culture. The low canopy of the rubber plantation, with its absence of understorey, the proximity of an almost continuous belt of breeding-places, and the early-morning visits of the tappers to the rubber-trees, together present an optimal opportunity to *Chrysops* for the taking of infective blood-meals. The small number of the tappers and the absence of other food-supplies for the fly expose them to a high risk of infection, while the flies in their turn are also exposed to a high risk of infection with *L. loa*. The circumstances accompanying each stage of this life-cycle of *L. loa* thus tend to expedite transfer.

"The life of the women in the rubber estate, who spend all their time in the village clearing and need never enter the rubber-trees, is correspondingly modified to present a minimal opportunity for transfer. In the village in the rain-forest, on the other hand, the women constantly enter the forest to collect their water and firewood or to farm their small patches of cultivated land."

In the naturally developing market-town of Kumba it was found that the development of infections with *L. loa* shown by children attending school in the Fiango area proceeds at the same rate but is only half that of the children attending the Basel Mission School. The following differences in the conditions of transfer can be held to account, in part at least, for the difference in the infection rates. The children at the Kumba Basel Mission School spend their day in an area close to the rain-forest, where *Chrysops* resting-places are plentiful and where there is ample opportunity for the flies to take blood-meals from man or from the canopy-dwelling monkeys. Since the inhabitants of this area are predominantly forest-dwellers, mostly Bafors, their infection-rate and their infectivity to the fly are likely to be high [KERSHAW, this *Bulletin*, 1951, v. 48, 574]. Of the adult monkeys of all species in the region, about one-third are infected with *Loa* species. In contrast, the children at Fiango are well separated from the rain-forest by a wide belt of farm mosaic and broken forest. Little is known of the ability of *Chrysops* species to cross clearings, but it is known that flies are so rarely seen in the area where the school is situated that their occurrence is considered worthy of note. "It is not yet known whether breeding-places are common in the flatter forest nearby. There is, no doubt, an adequate source of blood-meals for the *Chrysops* on the edge of the rain-forest at the periphery of the farm-lands from those farmers who cultivate the outlying strips, but they are mostly from the north—grass-lands people and Hausas—who are less likely to harbour *L. loa* than the Bafors. In addition to these

indirect effects caused by the clearance of the rain-forest, the large and increasing population of Fiango has a further important direct effect on the transmission of *L. loa* infections. The number of flies in the town is small in comparison with the number of persons exposed to risk. Consequently, the probability of the development, as a result of repeated exposure, of an infection sufficiently intense for microfilariae to appear in the peripheral circulation is less likely than among the Bafors. The population of Fiango, by reason of its low ratio of fly to man, is thus more likely to be able to reduce its risk of infection by mere dilution of the infective potential."

The author also discusses the influence of town and village evolution on the incidence and intensity of infections with *Acanthocheilonema perstans*, but he points out the difficulty of drawing conclusions from the available data until we have considerably more knowledge of the vector. R. M. Gordon

WOODRUFF, A. W. **Recent Advances in Tropical Medicine No. 2. *Loa loa* and Loiasis.** *West African Med. J.* 1952, Apr.-May-June, v. 1 (n.s.), No. 2, 45-55, 6 figs. [26 refs.]

A general review.

HAWKING, F. **A Histological Study of Onchocerciasis treated with Hetrazan.** *Brit. Med. J.* 1952, May 10, 992-4, 5 figs. on pl.

This interesting paper describes a histological study of nodules and skin biopsies, taken from patients suffering from onchocerciasis, before, during and after their treatment with hetrazan ("banocide"). The results recorded confirm and amplify Dr. Hawking's earlier work and should be studied in conjunction with his previous paper on this subject [this *Bulletin*, 1951, v. 48, 177].

The author summarizes the results of his present investigation as follows: "Patients infected with *Onchocerca volvulus* were treated with hetrazan, and subcutaneous nodules containing adult worms and samples of skin containing microfilariae were removed for histological examination.

"There was no significant difference between nodules from five untreated patients and those from nine patients treated with hetrazan, and there was no evidence that hetrazan had produced any adverse effect upon the adult worms.

"In skin samples from untreated patients, microfilariae in the corium usually did not excite any reaction; if reaction was caused it was mild in degree and chronic in nature.

"In skin samples after treatment with hetrazan there were numerous foci of intense acute inflammation. Microfilariae were often present in these foci, and showed evidence of degeneration and destruction; but sometimes they were also present in normal connective tissue without exciting a reaction.

"It is probable that the main action of hetrazan is to destroy microfilariae (probably by an opsonin-like effect), and that their destruction liberates some microfilarial product which excites an allergic reaction in the previously sensitized patient. Some microfilariae, however, are apparently less susceptible to the opsonin-like effect of hetrazan, and so they persist in the skin for long periods without doing visible harm.

"The allergic reaction provoked by hetrazan in patients with onchocerciasis can be used as an additional means of diagnosis."

The paper is illustrated by 5 excellent photomicrographs.

R. M. Gordon



JAMES, T. **A Case of Triple Infestation with *Trichuris trichuria*, *Ascaris lumbricoides* and *Enterobius vermicularis*.** *Glasgow Med. J.* 1952, May, v. 33, No. 5, 188-9, 1 fig.

This paper records the case of a child of 2½, with a history of wasting and anorexia who was admitted to the Duchess of York Hospital for Babies, Manchester, because of a long spell of intermittent passage of blood and mucus in the stool. She had been born in Offaly, in Ireland. In Manchester, ova of *Ascaris*, *Trichuris trichiura* and *Enterobius* were found in the stools and these are illustrated in three excellent photomicrographs. No *Trichuris* had been found in 327 microscopic examinations of faeces from children under 5 years in the Manchester hospital, though the other two worm infections were fairly common. Similar observations were made by the County Medical Officer of Offaly.

The author quotes the scanty literature on the incidence of *Trichuris* in Britain, which does not appear to have been studied comprehensively, possibly because the significance of *Trichuris* has been doubtful. There seems, however, to be an endemicity in Cornwall, dating to the days when metalliferous mines were operating and faecal contamination was common.

The source of infection in this case is unknown, and it appears to be the first record of such a triple infestation in Britain. [It is noted that *trichiura* is incorrectly spelt "*trichuria*" throughout the paper.]

H. J. O'D. Burke-Gaffney

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## DEFICIENCY DISEASES

HARRIS, R. S. **The Indigenous Edible Plants of Latin America.** *Internat. Ztschr. f. Vitaminf.* Berne. 1952, v. 23, No. 3, 404-14. [21 refs.]

"From the results of determinations of 14 nutrients in each of 1500 samples representing 250 varieties of edible plants collected in Mexico and Central America the following conclusions have been reached: (a) the composition and nutritional values of plants grown in different regions are not the same, (b) tropical and semitropical plants are often highly nutritious, (c) man can formulate his diet from a wide variety of foods, (d) peoples with well-established cultures generally use indigenous resources intelligently, (e) there are more varieties of edible foods in Central America than in the United States, (f) indigenous foods are less expensive, and (g) the attack on the food problems of undeveloped areas must be realistic. Considerable progress toward food independence in these areas can be made by an intelligent development of the indigenous edible flora."

THOMPSON, M. D. & TROWELL, H. C. **Pancreatic Enzyme Activity in Duodenal Contents of Children with a Type of Kwashiorkor.** *Lancet.* 1952, May 24, 1031-5, 4 figs. [20 refs.]

Previous studies from the medical school of Makerere College in Uganda have shown that failure of digestion and absorption plays an important part in the development of kwashiorkor [this *Bulletin*, 1948, v. 45, 633]. Diarrhoea is frequently associated with bulky unformed stools in which particles of undigested food may be seen. Further, at necropsy of cases of kwashiorkor, degenerative pancreatic changes are constantly found.

This study records the pancreatic enzyme activity of material obtained by duodenal intubation, which was radiologically controlled. In 24 normal controls (ages 9-51 months) the mean amylase activity was 2.92 units per ml. of material and the mean lipase activity was 3.84 units per 0.1 ml. of material. The corresponding means for 40 cases of kwashiorkor (ages 12-51 months) were 0.40 for amylase and 1.0 for lipase : on reintubation after treatment the means for these 40 cases rose to 4.33 for amylase and 3.88 for lipase. There were wide variations in the individual groups, especially for amylase activity, but the differences are statistically highly significant and in the case of lipase almost completely clear cut.

Treatment in different patients was with whole milk, skimmed milk, milk protein and a mixture of skimmed and whole milk, and all intercurrent infections were treated. Each of the forms of milk protein appeared effective. In the discussion it is suggested that a failure of pancreatic secretion activity is the most likely cause of the absence of enzyme activity. An addendum reports very low trypsin activity in the duodenal contents of 6 patients, in 3 of whom this was raised by treatment.

R. Passmore

RHODES, Katerina. **Some Observations on the Diet of Jamaican Children, with particular reference to Liver Disease.** *Brit. J. Nutrition.* 1952, v. 6, No. 2, 198-206, 2 figs. & 1 pl. [20 refs.]

The diets of 10 Jamaican children with liver disease, "serous hepatitis" [see HILL, RHODES, STAFFORD and AUB, this *Bulletin*, 1952, v. 49, 437] were compared with those of 5 apparently healthy Jamaican children. If 3.5 gm. protein/kgm. body weight is taken as a desirable standard, then the 5 controls had a mean intake of 72.5 per cent. of the standard (range 60-78) and the 10 children with liver disease had a mean intake of 32.6 per cent. of the standard (range 13-52.5). It is suggested that children with a low intake of protein, and especially animal protein, at first respond by a retardation of growth and later by a failure of the liver to synthesize essential enzymes and subsequently develop degenerative processes in the liver.

R. Passmore

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## HAEMATOLOGY

FOY, H., KONDI, Athena & HARGREAVES, A. **Response of the Megaloblastic Anaemias of Pregnancy to Animal Protein Factor.** Preliminary Report. *Brit. Med. J.* 1952, Apr. 19, 852-3, 1 chart. [15 refs.]

Animal protein factor (A.P.F.), also known as "aurofax", is a fermentation product of *Streptomyces aureofaciens* and a by-product of the manufacture of aureomycin. The preparation as supplied by the manufacturers contains, in addition to A.P.F., aureomycin, vitamin B<sub>12a</sub> and B<sub>12b</sub> and an "unknown factor".

A single case is reported. The patient, an African 5 months pregnant, never ate meat, she was icteric, the spleen, though not the liver, was enlarged, and the faeces contained scanty hookworm eggs. The following haematological values were found on admission: red blood cells, 1.31 million per cmm.; haemoglobin, 4.98 per gm. per cent.; packed cell volume, 15.7 per cent.; reticulocytes, 2.8 per cent., mean cell volume, 120 cu.  $\mu$ ; mean corpuscular haemoglobin, 37  $\mu$ gm.; mean corpuscular haemoglobin concentration, 31.4 per cent.; white blood cells, 6,000 per cmm.; Price-Jones curve displaced

slightly to the right of normal ; macrocytosis, 14.2 per cent. ; microcytosis, 0.0 ; mean corpuscular diameter,  $7.87 \mu$  ; mean corpuscular average thickness,  $2.43 \mu$ . The sternal marrow was hyperplastic containing giant stab cells and intermediate megaloblasts. Schumm's test was positive, and the serum bilirubin 2.6 mgm. per 100 ml.

In addition to an unmeasurable quantity of A.P.F. and " unknown factor " there was in the preparation administered daily 60 mgm. aureomycin,  $9 \mu\text{gm}$ . vitamin B<sub>12a</sub> and  $9 \mu\text{gm}$ . of vitamin B<sub>12b</sub>. On the seventh day of treatment a maximum reticulocyte response of 27 per cent. developed and was followed by adequate red cell and haemoglobin regeneration. No other treatment was given and during the 3 months following treatment there was no relapse.

The authors suggest that antibiotics may destroy micro-organisms which compete for accessory food factors or they may destroy other micro-organisms which produce toxins interfering with the utilization of accessory nutrients. Antibiotics which the authors have used in the treatment of megaloblastic anaemias might have produced their effect by virtue of some unknown haemopoietic factors which they contain rather than by any effects which they may have on bacterial flora. Although this may be the case with A.P.F. it is not likely to be so with penicillin. The authors have found that penicillin will produce its effects in the megaloblastic anaemias only if given in small doses—not more than 200,000 units twice daily by the intramuscular route, and not more than 125,000 twice daily by the oral route. Given in greater amounts than these it is haemopoietically ineffective (FOY and KONDI, unpublished). If the effects of penicillin were due to its content of unknown haemopoietic factors then one would expect results from large as well as small doses.

The authors conclude : (i) That large doses of antibiotic probably not only clear the gut of micro-flora competing with the host for the supply of essential factors, but also destroy flora synthesizing these factors. (ii) That the haematological response in the case described may have been due to (a) changes in the bacterial flora of the gut brought about by the antibiotic present in the A.P.F. ; (b) an unknown haemopoietic factor present in the A.P.F. ; (c) the small amount of vitamin B<sub>12</sub> present in the A.P.F. ; or (d) " sparing action " of the aureomycin on the vitamin B<sub>12</sub>.  
A. W. Woodruff

RAPER, A. B. **Sickle Cell Inheritance in a Case of Disputed Paternity.** *East African Med. J.* 1952, Apr., v. 29, No. 4, 125-7.

TOSTESON, D. C., SHEA, Ethel & DARLING, R. C. **Potassium and Sodium of Red Blood Cells in Sickle Cell Anemia.** *J. Clin. Investigation.* 1952, Apr., v. 31, No. 4, 406-11, 5 figs. [20 refs.]

CAMINOPETROS, J. **The Sickle-Cell Anomaly as a Sign of Mediterranean Anaemia.** *Lancet.* 1952, Apr. 5, 687-93, 12 figs. [39 refs.]

" The haemolytic anaemia of the peoples of the eastern Mediterranean area has to be distinguished from that of the Negroes of Africa and America." Individual cases of haemolytic anaemia with sickle cells have been reported repeatedly from Greece and Italy since 1936, but recently with the improved technique a large number of cases of sickle-cell anomaly has been found.

Two groups of patients were investigated by the author. The first group was from the village of Marcopoulo (population 4,000) and 2 neighbouring villages. There was no malaria or malnutrition in these villages nor had there been any interbreeding with Negro stock. Seven families were investigated. There were 7 cases of erythroblastic anaemia in these families, 3 acute and 4 chronic ; of these, 2 infants with the acute disease were investigated for the sickle-cell



anomaly and found negative, but one was re-examined 8 months later when he was 15 months old and found positive. Blood examinations in 3 of the 4 chronic cases showed the sickle-cell anomaly. Of 33 apparently healthy persons in the 7 families, 25, or 76 per cent., showed the anomaly.

The second group consisted of 18 families living in Athens. Of 6 patients with acute erythroblastic anaemia only one showed the sickle-cell anomaly and of 14 with the chronic disease all showed the anomaly. Of 51 healthy persons 35 (or 68.6 per cent.) showed the anomaly. All the acute cases were in infants of under two years of age. Of this last group, 13 out of 15 fathers and 12 out of 18 of the mothers showed the anomaly, in 7 families both parents were positive.

The sickle-cell anomaly occurs more regularly in the chronic form of erythroblastic anaemia of Cooley, and is not usually apparent during the first year of life although both parents may show it. A characteristic of the sickle-cell anomaly is the negative phase. This develops at irregular intervals for varying periods. These two facts probably account for the failure of paediatricians to report the sickling trait in many cases of erythroblastic anaemia of white persons, especially in infants.

The author concludes that the sickle-cell anomaly is common to both Cooley's erythroblastic anaemia of white people and to the "erythroblastic" anaemia of Negroes. Other common features are target cells, decreased fragility of the red cells, ulcers on the legs, and bony changes of the skull.

He attributes erythroblastic anaemia of white people to an admixture of mongol blood during invasions from Asia, and suggests that the name "drepanocytic anaemia of the Eastern Mediterranean" be applied to the latter disease.

L. E. Napier

BALOGH, G. M. K. **Familial Erythroblastosis (Cooley's or Mediterranean Anaemia) with Familial Hypercholesterolaemia.** *Pakistan J. of Health.* 1952, Jan., v. 1, No. 4, 1-20, 26 figs. & 5 graphs. [14 refs.]

Two abnormalities are described in a Punjab family. The mother and one son suffered from mild Cooley's anaemia, the remaining two children, a son and a daughter, showed the disease in its severe form. The father, a first cousin of the wife, had a mongoloid facies, but, though mildly anaemic, showed no other symptoms of Mediterranean anaemia.

All 5 members of the family suffered from hypercholesterolaemia.

The paper is illustrated with 2 photographs and 24 skiagrams.

H. Lehmann

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## VENOMS AND ANTIVENENES

WOODWARD, S. F. **Notes on West African Snakes.** *West African Med. J.* 1952, Apr.-May-June, v. 1 (n.s.), No. 2, 59-62.

This article, short though it is, imparts a great deal of information. It is, itself, too condensed to permit of abstract. The author, Dr. Woodward, is well known as a herpetologist and his statements are, therefore, authoritative. There is a widespread belief that certain snakes, the Mamba among them, will attack man unprovoked, but Dr. Woodward states that in his 20 years' experience he has never known an instance; perhaps it occurs only when the snake is cornered or has young with it, for, as Shakespeare tells us "Even doves will peck in safeguard of their brood". Another popular fallacy for which

he can find no support is that snakes mesmerize their prey. Lastly, he stresses the fact that it by no means follows that a poisonous snake has, in biting, necessarily injected its venom. The venom may have been already exhausted or the snake may be one of the *Opisthoglypha*, with the poison fangs behind the maxillary biting teeth. The article gives an excellent summary of the snakes of West Africa.

H. Harold Scott

## DERMATOLOGY AND FUNGUS DISEASES

AJELLO, L. **The Isolation of *Allescheria boydii* Shear, an Etiologic Agent of Mycetomas, from Soil.** *Amer. J. Trop. Med. & Hyg.* 1952, Mar., v. 1, No. 2, 227-38, 5 figs. [58 refs.]

In a preliminary report on the isolation of *Histoplasma capsulatum* and *Allescheria boydii* from soil, AJELLO and ZEIDBERG [*Bulletin of Hygiene*, 1952, v. 27, 338] described the method of inoculating mice with soil washings and recovering the pathogenic fungi in culture from the organs of the inoculated animals. The addition of hog's gastric mucin to the soil washings to give a concentration of 2.5 per cent. increased the infectivity of the fungi for the animals.

The present report relates to the same experiments but it deals only with *Allescheria boydii*. This fungus, found chiefly in its imperfect form (*Monosporium apiospermum*), is an important cause of mycetoma, and the author has reviewed the literature on this type of Madura foot and has tabulated its geographical distribution.

In all, 194 samples of soil from 41 farmsteads in Williamson County, Tennessee, were examined, and 4 strains of *A. boydii* were isolated, 3 of these with the aid of the gastric mucin technique. Although the fungus could be isolated repeatedly from the same sample of soil by inoculation into mice, all attempts to isolate it by direct culture from the soil, by means of dilution methods, failed.

The 4 strains isolated all presented the same characters and developed in culture as greyish-white, floccose colonies with a brownish-grey pigment on the reverse side, after 2 weeks on dextrose agar. Asexual reproduction was by ovoid conidia borne acrogenously and singly on the tips of hyphae or short lateral branches. The conidia measured  $7.3\mu$  by  $4.4\mu$  on the average, but their size was influenced by the quality of the culture medium. Sexual reproduction was represented by closed perithecia which were dark-coloured and spherical, measuring from 50 to  $90\mu$  in diameter. When these were crushed, masses of elliptical ascospores, measuring 5.0 to 6.5 by  $3.4\mu$ , escaped through the ruptured wall; intact asci were difficult to find.

Intraperitoneal injection into mice of spore suspensions of the soil strains of *A. boydii* and other strains from mycetoma, did not kill the animals or cause any gross lesion, but the living fungus could be recovered from their tissues 2 weeks after inoculation. However, when gastric mucin (2.5 per cent.) was added to the injection the animals died of the infection within one week. The organs showed no gross lesion but, on microscopical examination, germinating spores and proliferating mycelial filaments could be found in the liver and spleen.

A valuable addition to this report is a tabulated review of the published records of isolations of pathogenic fungi from saprophytic life in nature.

J. T. Duncan

## TROPICAL OPHTHALMOLOGY

BUDDEN, F. H. **Blindness in Northern Nigeria.** [Correspondence.] *Brit. Med. J.* 1952, June 7, 1248.

The author, from Jos, Northern Nigeria, refers to the memorandum by DODDS from Lagos, relating to blindness in Southern Nigeria [this *Bulletin*, 1952, v. 49, 646]. He also has been making similar surveys of the general population, schoolchildren and prisoners in some small areas of Northern Nigeria. His classification was similar to that of Dodds, but he subdivided the groups "leucoma, phthisis and staphyloma" into those with a history of (a) *bakwondoro*, which covers chickenpox, measles and septic skin conditions, (b) smallpox and (c) local eye disease only. Multiple lesions were common. Trachoma was the commonest cause of blindness found and accounted for 46/144 patients blind in both eyes and 28/130 blind in one eye. The incidence increased as one travelled north towards the desert. Onchocerciasis was the second commonest cause (39/144 and 10/130 respectively): its high incidence tends to be localized to certain areas. Senile cataract accounted for 18/144 cases, as compared with the much higher figure of 115/356 in Dodd's series: those with cataract, however, probably attend hospital in Lagos readily because of the facilities there. Trauma is a common cause of unilateral blindness (17/130 cases). No cases seen by the present author could be attributed to vitamin deficiency.

The results are shown in a table, which indicates, among other points, that the incidence of (a) (b) and (c) above were respectively 5, 4 and 10 in 144 bilateral cases and 10, 10, 28 in 130 unilateral cases. In 4 bilateral cases, there was primary optic atrophy due to injections for trypanosomiasis.

It is clear that trachoma and onchocerciasis were commoner causes of blindness than they were in the Lagos series.

H. J. O'D. Burke-Gaffney

SARKIES, J. W. R. **Ophthalmoplegia following a Scorpion Bite.** *Brit. J. Ophthalm.* 1951, Aug., v. 35, No. 8, 502-4, 2 figs.

A case of a complete ocular motor palsy in an African in Accra following a bite on the right eyebrow by a small grey scorpion is reported. There was acute pain at the site of the bite for some hours and gross swelling around the eye which lasted for about a month. The palsy occurred immediately after the scorpion bite. The case reported was evidently one of peripheral neuritis of the third cranial nerve.

The mechanism by which the lesions was produced was largely conjectural, the spread probably being from the cavernous sinus to the oculo-motor nerve in the middle cranial fossa. The result of successful surgical treatment is described.

E. O'G. Kirwan

FUCHS, A. **Peculiar Scars of the Upper Lid, a New Type of Disease in China.** Reprinted from *Urologic & Cutaneous Rev.* 1951, v. 55, No. 4, 213-15, 2 figs.

The author has observed that many Chinese of every social status have scars on their upper eyelids. These scars are superficial, flat, non-adherent, "2-3 cm long and 0.3-0.5 mm broad" [presumably 3-5 mm. broad]: they "often disclose excrescences of skin, similar to those which are sometimes seen as a congenital malformation in front of the ear". They are always on the temporal half of the upper lid and may extend on to the temple. No significance has



been attached to these scars by ophthalmologists in China. Various suggestions have been made for the origin : these include furunculosis, the pinching up of a fold of skin in a split bamboo to cure entropion, damage to the eyelid by the application of caustic solutions.

The author discards these theories. "A certain similarity exists between these very thin superficial scars and those which are seen in the Near East as result of an Aleppo—(Bagdad-, Biskra-) boil, a Leishmaniasis of the cheek especially on the os zygomaticum, but also on other parts of the face and body. The fresh cases of this very common oriental sore, disclose granulomata which ulcerate and lead slowly to scar formation. The scars of Aleppo-boil which I saw very frequently in the Near East did show occasionally excrescences of the skin, similar to those which are very common in the scars of the upper lid, in China."

The author suspects that these peculiar scars are the "sequel of a specific parasitic disease somewhat related to Leishmaniasis". He adds "perhaps, also, mosquitoes may be the transmitter".

[The author provides no support for his most improbable suggestions as to the nature and cause of these scars.]

L. E. Napier

FUCHS, A. **Peculiar Scars of the Upper Eyelids : a New Type of Disease in China.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1952, Jan., v. 46, No. 1, 63-4, 1 fig.

This covers the same ground as the above.

AMIES, C., MURRAY, N. L., SCOTT, J. G. & WARREN, R. St. H. **Trachoma in the South African Bantu. A Survey in Sekukuniland.** *South African Med. J.* 1952, Apr. 26, v. 26, No. 17, 362-3, 9 figs. (7 coloured on pl.).

It has been established that there are many cases of trichiasis, entropion and blindness among the South African Bantu in the Northern Transvaal. To decide whether trachoma was implicated, a survey was made at the Jane Furse Memorial Hospital and surrounding districts of Sekukuniland 200 miles N.E. of Johannesburg.

A total of 503 children ranging in age from one month to 18 years were examined. Infection with trachoma was found in 87 per cent. of the children. Only 68 cases (13 per cent.) had apparently normal lids. A random sample of 47 of these apparently normal children were examined with a lens and 38 were found to have pannus, indicating that trachoma had healed without scarring but had left the diagnostic blood vessels in the cornea. These 38 cases raised the incidence to 94 per cent.

The findings in children of Stage I, II and III trachoma (each stage showing pannus) in an area where trichiasis and entropion was known to be rife, was clinical proof of trachoma. In a total of 109 children of Stages I, II trachoma, Halberstaedter-Prowazek inclusions were found in 25 cases; inflammatory exudate in 81; Koch-Weeks infections in 70; *H. influenzae* infection in 12 cases. No gonococcus or pneumococcus infections were found.

Photographs of clinical trachoma and of inclusion bodies are presented to prove that trachoma existed among the South African Bantu. [See also this *Bulletin*, 1952, v. 49, 309.]

E. O'G. Kirwan

DE ANDRADE, L. **Trachoma. Diagnosis and Treatment.** *Brit. J. Ophthalm.* 1951, Oct., v. 35, No. 10, 601-6, 2 figs. [12 refs.]

In this article the author, from Lisbon, discusses the diagnosis and treatment of trachoma. He is of the opinion that the diagnosis of early trachoma can

be made with fair certainty if the clinical, laboratory and histo-pathological findings are considered together, the following being the important features in each group :—

1. Clinical findings.—The presence of granulations in the upper part of the conjunctival sac ; incipient pannus ; early scarring in some cases and resistance to the general forms of treatment.

2. Laboratory findings.—The presence of Prowazek's inclusion bodies and lymphocytosis.

3. Histopathology.—The presence of granulations with a central epithelial zone and a peripheral lymphocytic zone ; and the presence of plasma cells, Leber's cells and vesicular cells.

In spite of the recent developments of chemotherapeutic and antibiotic preparations, the classic treatment of trachoma by means of copper, silver nitrate and the sulphonamides must be in some part retained. The mechanical destruction of the trachomatous granulations and the action of diathermy coagulation and irradiation are local measures which remain of great value in controlling the disease and limiting its late manifestations.

Aureomycin applied locally and given systemically for periods varying from 10 days to 2 months did not cure patients with trachoma in the first, second and third stages. In most cases there was a subjective improvement probably due to the disappearance of secondary infection. If the conjunctival granulations were improved or cured by aureomycin, they were not of trachomatous origin.

The author presents a simple scheme which has been in use for some years at the Ophthalmological Institute of Lisbon for the treatment of trachoma in its various stages.

E. O'G. Kirwan

SORSBY, A. **Specific Treatment of Infections of the Eye.** *Brit. Med. J.* 1951, Sept. 1, 539-41.

Present-day treatment of infections of the eye is highly specific and a clear understanding of the infective lesions of the eye as distinct from the inflammatory reactions is therefore essential if any good results are to be obtained. The sulphonamides, penicillin and streptomycin, used locally, are not free from irritative reactions. The sulphonamides are of limited value in ocular infections except trachoma ; the irritative reactions are therefore of no great importance. Those that occur with penicillin are almost entirely due to the use of impure brands. If white crystalline penicillin is used reactions are exceptional with drops and almost equally exceptional with ointments if a suitable ointment base is employed. A simple base such as 90 per cent. petroleum jelly and 10 per cent. liquid paraffin gives excellent results. Reactions are still less likely if the penicillin is incorporated in powder form into the base and not first dissolved. Streptomycin is rather more apt to cause irritation but this is not likely to occur except with prolonged use.

In purulent and mucopurulent conjunctivitis if the infection is not well under control within 24 hours of adequate penicillin or sulphonamide therapy, it may safely be assumed that it is due either to Gram-negative bacilli or insensitive strains of organisms which are normally sensitive to these drugs. In virus infections of the cornea which are exemplified by epidemic keratoconjunctivitis and superficial punctate keratitis and in chronic conjunctivitis, persistent treatment with sulphonamide and penicillin only aggravates matters, for drug irritation is added to the inflammatory reaction. Ophthalmia neonatorum, most commonly caused by the staphylococcus and in 20 per cent. of cases by the gonococcus, is treated by two alternate methods. The easier, though somewhat slower, method is the oral administration of sulphonamides.

Penicillin locally gives incredibly rapid results but calls for considerably more nursing care. As a routine method, where no special facilities are available, treatment by oral sulphonamides is the method of choice. In all cases, atropine sulphate drops, 1 per cent., are instilled if the cornea is hazy. Sulphonamide is administered as a tablet of sulphamerazine (0.5 gm.) crushed into powder and given by the mouth in a teaspoonful of water or milk. The sulphonamide in doses of 0.25 gm. is continued for 8 hours until 48 hours after clinical cure. Local treatment consists in irrigation with isotonic saline solution every 3 hours during the first day in cases with profuse discharge. After irrigation medicinal paraffin is instilled as a precaution against sticking together of the lids.

Swelling of the lids generally subsides within 12 hours and the purulent discharge disappears within 24 hours.

In penicillin therapy a drop of penicillin in a concentration of 10,000 units per ml. is instilled into the conjunctival sac; one drop of the solution is instilled every minute for 30 minutes. At the end of this time there is generally little or no discharge. Penicillin drops are continued 6 times at 5-minute intervals followed by a similar number of instillations at  $\frac{1}{2}$ -hour, hourly, and 2-hour intervals: this gives a total of 22 hours of treatment. Crystalline penicillin only should be used for making up the drops.

For the purulent conjunctivitis in adults there is no fundamental difference in treatment, from that employed for ophthalmia neonatorum except that if oral sulphonamide is used, full adult doses should be given.

Trachoma is still the largest blinding disease in the world. Mechanical expression of follicles is still an important part of present-day treatment of trachoma. After expression, the fornix should be painted with 30 per cent. sodium sulphacetamide daily for a month or so. Sulphacetamide ointment 6 per cent. in a base consisting of 90 per cent. petroleum jelly and 10 per cent. liquid paraffin should be used 3 to 4 times daily. When the cornea is involved, atropine sulphate drops 1 per cent. are instilled daily (up to 3 times) to keep the pupil dilated. If there is a secondary infection of the conjunctiva when the patient is first seen, full doses of oral sulphonamides for 3 to 4 days should be given before undertaking expression of the follicles and local therapy.

The value of aureomycin and chloramphenicol in trachoma still remains to be assessed.

In infections of the cornea every case should be treated at once on the assumption that it is caused by a penicillin-sensitive organism. If, after 24 hours, penicillin therapy has not produced a marked improvement and the culture shows no organisms or reveals Gram-negative organisms, the penicillin should be discontinued.

For hypopyon ulcer the best results are obtained by subconjunctival injection of penicillin: after the eye is adequately cocainized the subconjunctival injection can be easily given. This contains 1,000,000 units of crystalline penicillin dissolved in 10 min. (0.6 ml.) of sterile water and 5 min. (0.3 ml.) of adrenaline 1 in 1,000. The second injection if required can be given after 24 hours. Maintenance treatment is continued by instilling penicillin ointment containing 100,000 units per gm. at intervals of 2 hours for a further 2 to 3 days.

Corneal ulcer due to Gram-negative bacilli can be satisfactorily treated by subconjunctival injection of 0.5 gm. of streptomycin in a manner similar to penicillin injection. Two or 3 injections at intervals of 24 hours are necessary. Maintenance treatment should be continued with streptomycin ointment having 0.1 gm. per gm. at 2-hour intervals for 2 to 3 days.

Chronic simple blepharitis is generally due to a low-grade infection by penicillin-sensitive organisms. Treatment consists of removing the scales or scab with cotton-wool swabs moistened either with hydrogen peroxide or



sodium bicarbonate lotion. When the lid margins are clean, penicillin ointment containing 1,000 units of crystalline penicillin per gm. should be applied nightly for a fortnight or so. If penicillin treatment fails, the alternative is to paint liquor tinctorum B.P.C. on to the lid margin. *E. O'G. Kirwan*

DUKE-ELDER, S., AINSLIE, D. & BOASE, A. J. **Aureomycin in Ophthalmology (A Preliminary Report).** *Brit. J. Ophthalm.* 1950, Jan., v. 34, No. 1, 30-37.

After a general introduction by Duke-Elder, the results obtained in 33 cases of eye infections treated with aureomycin are given by Ainslie and the method of administration is described.

Cases of chronic irido-cyclitis did not appear to benefit with the possible exception of a case of recurrent hypopyon uveitis. Dendritic ulcers and superficial punctate keratitis did not respond. One case of keratitis disciformis appeared to benefit. A case of blepharitis due to non-penicillin sensitive staphylococcus had benefited initially. An infection with *H. influenzae* improved while under treatment. An example of inclusion conjunctivitis was treated and showed marked improvement.

One case of herpes ophthalmicus and one case of sympathetic ophthalmia were treated without benefit.

Boase describes results in 8 cases of trachoma, with the use of conjunctival instillation of aureomycin. Highly satisfactory results followed the simple routine of 1 drop every 4 hours.

Details are given of the cases and their treatment.

*E. O'G. Kirwan*

TROPE, R. A. **Trachoma. Aureomycin (Oily Suspension) in its Out-Patient Treatment. A Preliminary Report.** *South African Med. J.* 1950, Nov., 18, v. 24, No. 46, 954-5.

As a result of the encouraging results in 8 cases of trachoma treated with the aqueous solution of aureomycin [above], Trope used this drug in the treatment of trachoma in the Krugersdorp Hospital, South Africa. The results were very disappointing, which he attributed to the fact that all the patients were treated as weekly out-patients and that the antibiotic activity of aureomycin lasted only from 12 to 48 hours.

Later he used a suspension of aureomycin hydrochloride in castor oil in the following form: aureomycin hydrochloride 50 mgm. ol. ricini 10 cc. The drops are instilled into the eyes every hour. Eight cases of typical trachoma varying from stages I to IV were treated with extremely gratifying results.

An important aspect of this treatment is that it allows domiciliary treatment and as the suspension retains its antibiotic activity, the aureomycin retains its potency unimpaired. Cases of trachoma in rural areas can be treated, at great distances from hospitals, where daily observation cannot be maintained.

*E. O'G. Kirwan*

TROPE, R. A. **Topical Aureomycin (Oily Suspension) in Ophthalmology. First Reports on 47 Cases.** *South African Med. J.* 1951, Jan. 27, v. 25, No. 4, 53-4.

Following the dramatic results obtained by the author [above] in treating cases of trachoma with the topical administration of aureomycin in oily suspension [above], he now reports the results of 5 months of trial with the drug in other inflammatory conditions of the eye. The aureomycin was used in a 0.5

per cent. suspension in castor oil and administered by instillation into the conjunctival sac. To none was the drug given by mouth. Forty-seven patients were treated, of which 17 were suffering from trachoma in the various stages while the remainder were inflammatory conditions of uncertain aetiology.

Where the eyelids, cornea and conjunctiva were affected the results have been very gratifying. In 3 cases in which the inner tissues of the eye were involved there appeared to have been no effect.

Notes are given of the results in each of the various conditions, which included conjunctivitis, blepharitis, ulcers, keratitis, and irido-cyclitis. *E. O'G. Kirwan*

SARKIES, J. W. R. **Aureomycin in Trachoma.** *Brit. J. Ophthalm.* 1951, Sept., v. 35, No. 9, 549-52.

The results of treatment of trachoma with aureomycin and sulphadiazine are compared in a total of 62 cases.

Aureomycin was used in the form of an ointment 0.1 per cent. (Lederle) and was inserted under the upper and lower lids 6 times daily; in 2 of 31 cases aureomycin was also given by the mouth, the dosage being 1.5 gm. daily for 5 days. Sulphadiazine was used in a 30 per cent. ointment in 31 controls and was inserted in the same way but only once daily.

Symptomatic relief was noted in all those not complicated by entropion.

With both methods the improvement appeared to be due to the relief of the secondary infection and not to cure of the trachoma. The slightly greater efficacy of aureomycin appears to be due rather to a wider antibiotic range against secondary invaders than to a specific effect on the trachoma virus.

*E. O'G. Kirwan*

SHAH, M. A. **Aureomycin in Trachoma.** Reprinted from *Brit. J. Ophthalm.* 1951, Jan., v. 35, 50-52.

The author presents a report of 75 cases of trachoma treated by aureomycin (Lederle). These cases comprise 54 men and 21 women of different age-groups ranging between 6 and 70 years of age and suffering from trachoma with unmistakable pannus. In 61 the pannus was of the fine type and in 14 cases the coarse type. Two-thirds of the patients were in the second stage of trachoma (MacCallan's classification) and the remainder were in the third stage.

Aureomycin was used in the form of watery borate drops and these were instilled into each eye every 2 hours. In the majority of cases the duration of treatment lasted from 8-14 days. In all but 2 there was dramatic improvement, the eye becoming white within 5 to 7 days.

Aureomycin like other antibiotics and chemotherapeutic drops relieves the symptoms of irritation, lachrymation and redness and the results obtained were more dramatic and the duration of treatment shorter.

It failed, however, to produce any beneficial effect on the pannus in 92 per cent. of the cases.

*E. O'G. Kirwan*

SIGGIA, S. & MAMOLA, P. Essais de traitement du trachôme avec pénicilline procainée en huile additionnée de monostearate d'aluminium. [**Treatment of Trachoma with Procaine Penicillin in Oil with Aluminium Monostearate**] *Congrès Internat. Hyg. et Méd. Méditerranéennes Alger*, 3, 4, 5, Avril 1950. 155-8.

## TROPICAL ULCER

CASTELLANI, A. Quelques observations et considérations sur les "ulcérations de la jambe" les plus fréquentes dans les tropiques et les subtropiques, avec description de deux ulcérations peu connues: *Macrouleus perstans* et *Ulcus tropicaloides*. [Observations on Less Frequent Leg Ulcers in Tropical and Subtropical Regions, with a Description of Two Little-Known Forms, *Macrouleus perstans* and *Ulcus tropicaloides*] *Bull. Soc. Path. Exot.* 1952, v. 45, No. 2, 273-88, 9 figs. on 6 pls.

See also this *Bulletin*, 1948, v. 45, 1116; 1951, v. 48, 583.

BERTRAND, M. Ulcères phagédéniques. Considérations sur l'épidémie de 1943. [Phagedaenic Ulcers. A Study of the 1943 Epidemic in Algeria] *Maroc Méd.* 1950, Feb., v. 29, No. 297, 209-19. [63 refs.]

This is an historical study of phagedaenic ulcer in French North Africa and an account of an outbreak in the army in Algeria in 1943. Phagedaenic (or tropical) ulcer appears to have been introduced into Algeria from Madagascar in 1895 but did not find a suitable environment for it to become endemic. The 1943 outbreak now studied was aestivo-autumnal. The first cases occurred in September, the peak was reached in October, and no cases occurred after December, the wane coinciding with the onset of the cold weather. In all, 393 cases were seen in a period of 13 weeks, and in 384 of these the lower limbs were affected. Adenitis and septicaemia were not seen, and re- and auto-infection were very rare. Sulphonamides and penicillin were found to be of great service but in spite of them healing took 1 to 2 months. The rôle of Vincent's organisms is discussed but no definite conclusion as to their importance is reached. There is a suggestion that a streptococcus is the primary cause of the lesion. Unhygienic conditions and malnutrition, especially vitamin deficiency (A and C) were found to be indisputable factors in the outbreak.

H. G. Calwell

KOERBER, R. Contribution à l'étude de l'ulcère phagédénique en Afrique Occidentale Française. [Contributions to the Study of Phagedaenic Ulcer in French West Africa] *Maroc Méd.* 1950, Feb., v. 29, No. 297, 224-8. [16 refs.]

Tropical ulcers are a major problem in tropical medicine, and the extent of the problem is measured by the figures given in this paper. In the French West African territories in 1941 and 1942, 2.6 per cent. of all out-patients at hospitals and 7 per cent. of all in-patients suffered from phagedaenic ulcers. The incidence was highest in regions of humidity and moderate heat, and in the members of plantation and other labour forces who were exposed to trauma of the lower limbs, and whose diets were sometimes unsupervised and lacking in vitamin C. *Fusiformis fusiformis* and "*Borrelia phagedenis*" were found constantly in the ulcers and other organisms such as streptococci, staphylococci, enterococci and coliform bacilli frequently. Rapidity of ulceration, slowness of healing, and failure ever to heal spontaneously, were usual. Malignant changes occurred in 7 of a series of 108. Frequent complications were anaemia, gangrene of muscle, periostitis and osteomyelitis. Many forms of treatment are mentioned:—

1. Cleansing by a drip of Dakin's solution used for 3 to 4 hours at a time until the ulcer is clean.
2. Sulphonamide paste made with cod liver oil.
3. Penicillin locally and parenterally.
4. Tyrothricin (greatly praised).



Other procedures of a more heroic nature are lumbar sympathectomy or novocaine injection of the lumbar sympathetic chain to produce vaso-dilatation and facilitate cicatrization. The general treatment of the patient is not forgotten and the conclusion is of the most practical, namely that all wounds, however trivial, should be properly attended to, for if they are they will not be the forerunners of phagedaenic ulcers.

H. G. Calwell

CLAVIÉ, L. C. Traitement rapide de l'ulcère phagédénique. [**A Rapid Treatment of Phagedaenic Ulcer**] *Maroc Méd.* 1950, Feb., v. 29, No. 297, 232-4.

After a warning against mistaking a syphilitic gumma for a tropical ulcer and the converse, Clavié describes a method of ulcer treatment which he claims to be easily applicable in all circumstances, economical of material, and rapid and constant in efficacy. It is based on the poor resistance to heat of the spirillum, which organism is always found in these ulcers. The treatment comprises:—

1. Lavage with a 1/3,000 solution of potassium permanganate at 50°C. for 5 minutes.
2. Immediate drying with 95° alcohol containing 5 per cent. camphor.
3. Dusting with sulphonamide powder.
4. Application of ointment to the surrounding skin to prevent secondary impetigo.

5. Dressing with a compress soaked in normal saline, the compress to be moistened every 3 hours. The patient should rest with the leg elevated.

After 3 or 4 hot lavages the ulcer becomes clean and lavage may be stopped. When granulation starts the sulphonamide and alcohol may be stopped, and drying by ether followed by dusting with starch iodide and later vitaminized (A and D) Lassar's paste undertaken. More than 200 patients were treated, and cicatrization was obtained after 8 to 10 thrice-weekly treatments. The concurrent use of penicillin did not confer any added advantage.

H. G. Calwell

MONTESTRUC, E. & SAINT-CYR, C. La thérapie tissulaire, suivant la méthode de Filatov, dans le traitement des ulcères tropicaux des membres inférieurs. [**Filatov's Tissue Transplants in the Treatment of Tropical Ulcer of the Leg**] *Bull. Soc. Path. Exot.* 1952, v. 45, No. 2, 182-5.

Filatov's method is becoming increasingly popular with many workers for the treatment of tropical ulcer. The present authors, in Martinique, have used amniotic grafts, as placental extracts were badly tolerated. Portions of amnion were kept at 4°C. for 6 days in 3 per cent. sodium salicylate, cut in pieces measuring 4×4 cm. and autoclaved for 1 hour. Rigid bacteriological control was employed. After local anaesthesia with 1 per cent. scurocaine, a 2 cm. incision was made in the outer aspect of the thigh, the graft inserted and the wound closed with clips. The graft was renewed once or twice at intervals of 15 days if required.

Details are given of 22 cases in patients of 10 to 69 years, whose ulcers had been present from 15 days to 26 years. There were 16 successes, with cicatrization in 15 days to 1½ months, 4 improvements and 2 failures. No severe complications, allergic reactions or other side-effects were seen, and in all cases the transplant was absorbed in 15 days. It is added that success was also obtained in a post-operative fistula of the prostate, in burns and in a case of osteomyelitis.

The authors consider that Filatov's technique is the most successful form of treatment for tropical ulcer. [See also this *Bulletin*, 1950, v. 47, 403.]

H. J. O'D. Burke-Gaffney

CROZES & GUTH. Traitement des ulcères phagédéniques par électro-coagulation diathermique. [**Treatment of Tropical Ulcer by Diathermic Electro-Coagulation**] *Maroc Méd.* 1950, Feb., v. 29, No. 297, 229-31, 1 fig.

The following is a translation of the authors' summary :—

In 29 cases especially examined and followed up microscopically, we have found :

In 18 cases complete and immediate disappearance of specific microorganisms and the development of an aseptic wound in a few minutes.

In 7 cases, disappearance of fusiform bacilli, with persistence of common bacteria in small numbers.

In 4 cases, rare fusiform bacilli and spirochaetes persisting, probably because of insufficient electro-coagulation. However, in these cases the ulcers improved.

The serious complications also disappeared completely, namely secondary haemorrhage, acute arthritis, extensive osteitis and death from cachexia and progressive diarrhoea.

H. J. O'D. Burke-Gaffney

### MISCELLANEOUS DISEASES

RUDRA, M. N., CHOWDHURY, L. M. & SINHA, S. P. **A Preliminary Report on the Treatment of Lathyrism with Parenteral Methionine.** *Indian Med. Gaz.* 1952, Mar., v. 87, No. 3, 89-91.

In 1947 BODIAN and MELLORS reported finding a decrease in creatine phosphate in regenerating neurones (*J. Biol. Chem.*, v. 167, 655) and Professor Rudra inferred from this that motor neurone degeneration such as occurs in lathyrism might be due to a local deficiency of creatine, and that this deficiency might be caused by methionine deficiency or due to disturbance of transmethylation [see also this *Bulletin*, 1951, v. 48, 198]. He, working with Chowdhury, also found that lathyrus peas, though rich in protein, had a low methionine content. Chowdhury, at Professor Rudra's suggestion, gave methionine intravenously to 5 patients suffering from lathyrism. The usual dose was 1 gm. daily for 4 days, two had an increased dose up to 2 gm. for the next 4-6 days. In two the treatment had to be stopped, temporarily at least, owing to lack of methionine. In 3, the gait improved; 3 showed no improvement in physical signs but the patients expressed themselves as better in general health. [This is published as a "preliminary" report; perhaps it is also somewhat premature, since so few cases have received the treatment and 2 of the 5 inadequately, and any improvement was only partial. Further reports will be awaited with interest.]

H. Harold Scott

### PROTOZOOLOGY : GENERAL

HOLZ, J. Versuche der Züchtung von Spirillen und einiger pathogener Protozoen in isolierten Backentaschen von Goldhamstern (*Mesocricetus auratus*). [**Cultivation of Spirilla and Protozoa in the Cheek-Pouches of Hamsters**] *Ztschr. f. Hyg. u. Infektionskr.* 1952, Feb. 1, v. 133, No. 6, 557-60, 2 figs.

The author describes an operation whereby the cheek-pouch of the golden hamster can be artificially isolated, by stitching its outlet, and used *in vivo* for

anaerobic cultivation of various micro-organisms, which are injected into the pouch through the skin. The inoculation of *Spirillum* (Koch's and Fortner's) resulted in scanty growth in the cavity, while trypanosomes, toxoplasms and leptospire were able to penetrate through the mucous membrane of the pouch, and could afterwards be recovered from the blood of the hamsters.

C. A. Hoare

LELONG, M. & DESMONTS, G. L'emploi du microscope à contraste de phase dans la réaction de Sabin-Feldman. [Use of Phase Contrast Microscope in Sabin-Feldman's Reaction] *C. R. Soc. Biol.* 1951, Nov., v. 145, Nos. 21/22, 1660-61.

As is known, Sabin-Feldman's dye-test for the diagnosis of toxoplasmosis is based on the fact that the toxoplasms when in contact with normal serum stain with alkaline methylene blue, whereas in immune serum they remain unstained. The authors have found that the differences between parasites exposed to the two sera can be observed without staining, by use of the phase contrast microscope. When examined with oil immersion, normal parasites are seen to have a very dense cytoplasm and appear as homogeneous bodies without visible structure, while at lower magnification they appear as bright refractile bodies against a grey background. On the other hand, in immune serum the body of the parasite acquires a coarsely granular structure and the nucleus becomes visible as a clear central zone; later the granules and nucleus become smaller, until finally the parasite may be reduced to a membrane containing particles in Brownian movement. These changes in the structure of the parasite, which are irreversible, correspond to the loss of stainability by methylene blue. Similar changes can be produced in toxoplasms by heating, by addition of antiseptics and by rough and prolonged shaking. [This would seem to indicate that immune serum also has a lethal effect on the parasites.]

It is pointed out that the serological test carried out by phase microscopy is easier and more reliable than the original dye-test: at high magnification with a dry lens, the grey crescentic toxoplasms filled with granules can be readily distinguished from the bright homogeneous crescents representing normal parasites.

C. A. Hoare

WESTPHAL, A. & BAUER, F. Weitere Untersuchungen und Betrachtungen zur Toxoplasmose-Komplementbindungsreaktion nach Westphal. [Westphal's Complement-Fixation Reaction in Toxoplasmosis] *Ztschr. f. Tropenmed. u. Parasit.* Stuttgart. 1952, Feb., v. 3, No. 3, 326-39. [16 refs.]

Continuing previous investigations [this *Bulletin*, 1952, v. 49, 320] on Westphal's modification of the complement-fixation reaction for the diagnosis of toxoplasmosis, the authors have compared the results obtained by this method and with Sabin-Feldman's dye-test in 170 hospital patients, bringing the total number of persons tested to 285. In 85 per cent. of cases the results of the tests were identical, in 6 they differed, while in 9 they were inconclusive. It is thought that the negative results might have been due to fluctuations of the titre in the course of the infection.

In view of the occurrence of positive reactions for toxoplasmosis in a number of other diseases, attention is drawn to the incompleteness of knowledge regarding the clinical manifestations of toxoplasmosis. The positive serological tests in such cases may actually point to an association of these complaints with toxoplasmosis, since the latter affects about 20 per cent. of the German population.

A comparison was made between mouse and guineapig antigens for the complement-fixation test. It was found that the former gave a higher proportion of positive reactions than the latter. This difference is said to be due



to incomplete purification of the murine antigen, in which traces of the host's protein are still present. On the other hand, guineapig antigen preparations appear to be free of extraneous protein, and are therefore more specific, on account of which it is henceforth proposed to use them exclusively for Westphal's complement-fixation test.

Parallel observations carried out with the intracutaneous test and the two other tests tallied well, though the correspondence between the complement-fixation and dye-test was closer.

C. A. Hoare

HEIN, W. Das Verhalten des Sabin-Feldman-Testes und der Westphal'schen Komplementbindungs-Reaktion bei der Lungentuberkulose. [**The Sabin-Feldman Test and Westphal's Complement-Fixation Reaction in Pulmonary Tuberculosis**] *Ztschr. f. Tropenmed. u. Parasit.* Stuttgart. 1952, Feb., v. 3, No. 3, 339-57. [34 refs.]

It has previously been shown that animals inoculated with the sputum of a patient suffering from relapsing pneumonia acquired a toxoplasmic infection, and that in two cases of pulmonary tuberculosis positive serological reactions for toxoplasmosis were obtained. These observations induced the author to extend the investigation, and he accordingly applied Sabin-Feldman's test and WESTPHAL'S complement-fixation test [for latter see this *Bulletin*, 1952, v. 49, 320] in 102 patients suffering from pulmonary tuberculosis. The reactions were positive in 59 cases (57.8 per cent.), while in 14 the results were inconclusive. In a lengthy discussion of these results, it is pointed out that this figure is considerably higher than the estimated incidence (20 per cent.) of toxoplasmosis in Germany, thus apparently pointing to the non-specific nature of the toxoplasmosis serological tests, comparable to the positive Wassermann reaction occurring in malaria, scarlet fever, virus pneumonia, etc. On the other hand, it is argued that the high percentage of tuberculous patients reacting positively to these tests might indicate that in tuberculosis or toxoplasmosis or both, conditions favouring coexistence with the other disease are present.

C. A. Hoare

REISS, H. J. & VERRON, G. Beiträge zur Toxoplasmose. [**Contributions to the Study of Toxoplasmosis**] *Deut. Gesundheitswesen.* 1951, June 7, v. 6, No. 23, 646-53, 10 figs. on 2 pls. [23 refs.]

Some account of the history of the comparatively recent discoveries regarding toxoplasmosis and the nature of the infecting protozoon introduces a description of 2 fatal cases of the disease in a new-born child and a female child aged  $1\frac{3}{4}$  years. The paper gives a full account of the histories, symptoms, clinical investigations, progress and findings at autopsy. The serological tests were positive and the causal protozoon was demonstrated in both cases.

The paper is illustrated by 10 photographs.

Treatment is not yet satisfactory. Aureomycin and chloramphenicol are considered by some to be of value in the visceral form of the disease. In animals large doses of the sulphonamides are said by Sabin to control the infection.

M. E. Delafield

STRAUB, W. Augenbefunde bei der mittels des positiven Sabin-Feldman-Testes nachgewiesenen Toxoplasmainfektion des Menschen. [**Eye Conditions in Man in Toxoplasma Infection demonstrated by the Sabin-Feldman Test**] *Deut. med. Woch.* 1951, July 6, v. 76, Nos. 27/28, 890-92, 1 fig. [24 refs.]

This paper on eye conditions caused by, or associated with, toxoplasmosis begins with some general description of the infection, knowledge of which has

so greatly increased in the last decade. The disease is now known to exist not only in tropical and subtropical countries, but also in Europe, including Scandinavia. Latent forms of the disease in pregnant women may cause abortion or still-births, and the new-born infant may have congenital deformities. In the adult, infection causes no symptoms which are definitely diagnostic, but may manifest itself in disorders of the liver and intestinal tract, exanthemata, and arterial disease. There is also in the adult a latent, so-called "chronic form" which has been stated by some observers to be common, as for example in Hamburg where 2 per cent. of the population are believed to be infected.

The most reliable diagnostic serological test is that of Sabin and Feldman.

There are then described, with illustrative case histories, the congenital eye conditions which may be found. The most common abnormality is bilateral central choroiditis, but microphthalmos, disseminated choroiditis, pseudo-retinitis pigmentosa, optic atrophy, irido-cyclitis, and lens opacities may be found.

Special investigation has been made of ocular conditions in the adult in toxoplasmosis. During 18 months, 73 eye patients among others who were tested by means of the Sabin-Feldman test gave a definitely positive result. The eye conditions found on examination were very varied—they included lesions of the choroid, haemorrhages in the fundus, and sub-retinal exudate, mostly in the central region. Changes in the blood vessels such as thrombo-angitis and arteriosclerosis were also noted. Optic neuritis was found in 3 cases. The serological test was positive in about half the cases of irido-cyclitis.

M. E. Delafield

GIROUD, P. & GAILLARD, J. A. Constatations morphologiques et anatomiques dans la toxoplasmose pulmonaire expérimentale du lapin. [**Morphological and Anatomical Findings in Experimental Pulmonary Toxoplasmosis of Rabbits**] *Bull. Soc. Path. Exot.* 1951, v. 44, Nos. 11/12, 730-34, 4 figs. (3 on 2 pls.).

In a previous paper [this *Bulletin*, 1952, v. 49, 726] the authors described a method of producing experimental pulmonary toxoplasmosis in rabbits. The lungs of the infected animals provided material for the present study. Smears of lung tissue stained by the May-Grünwald-Giemsa method revealed a heavy infection with toxoplasms comparable to that seen in smears of the peritoneal fluid from infected mice. The parasites were either free or intracellular, chiefly in macrophages. In addition to parasites like those occurring in mice, forms were seen which might be regarded as stages of development or as forms modified by the action of the host's cellular defence mechanism. These appear in the form of large bodies containing chromatin-like structures which are at first scattered, but later become concentrated. Finally the cytoplasm undergoes fission into a number of portions which become separated into distinct parasites of typical structure. These divide longitudinally and eventually rupture, releasing numerous toxoplasms. Sometimes the intracellular parasites appear to fuse, giving rise to the larger bodies mentioned above.

In sections of infected lungs, the histopathological picture points to interstitial bronchopneumonia resembling that described for human toxoplasmosis, and characterized primarily by changes in the reticulo-endothelial elements, with secondary alveolar lesions. The appearance of the parasites and the histopathological changes are shown in a number of figures.

C. A. Hoare

VANĚK, J. & JÍROVEC, O. Parasitäre Pneumonie. "Interstitielle" Plasmazellenpneumonie der Frühgeborenen, verursacht durch *Pneumocystis Carinii*. [**Parasitic Pneumonia. "Interstitial" Plasma-Cell Pneumonia due to *Pneumocystis carinii* in Little Children**] *Zent. f. Bakt.* I. Abt. Orig. 1952, May 12, v. 158, Nos. 1/2, 120-27, 5 text figs. & 7 figs. on pl. [28 refs.]

The English summary appended to the paper is as follows :—

"The authors observed 16 cases of special pneumonia in children aged about 3 months either premature or debilitated by sickness. It is the protozoon *Pneumocystis carinii* that is regarded responsible for this sickness which nearly always takes a fatal course. Part of its developmental cycle could be elucidated. *Pneumocystis* forms foamlike masses composed of parasites in alveoli and bronchioles. These parasites, which have a thick foamlike wrapping substance, are small uninuclear roundish or longish bodies reproducing by binary fission and finishing by forming eight-germinal sporogonies about 5 to 7  $\mu$  in size. Domestic gnawers such as rabbits and guinea-pigs as well as cats, dogs, sheep and goats are used by the parasites as reservoirs. The way of transmission is still unrecognized. The data obtained by MEER and BRUG (1942) who first found *Pneumocystis* as infectious agent in man, could to a considerable extent be completed. The identity of this affection with interstitial non-syphilitic pneumonia as described for the first time by AMMICH (1938) is shown."

## ENTOMOLOGY AND INSECTICIDES : GENERAL

[Papers on the toxic effects of insecticides in man are abstracted in the *Bulletin of Hygiene* under the general heading of Occupational Hygiene and Toxicology.]

FLOCH, H. & ABONNENC, E. Anophèles de la Guyane Française. [**Anophelines of French Guiana**] *Arch. Inst. Pasteur de la Guyane et du Territoire de l'Inini.* Publication No. 236. 1951, Aug., 91 pp., 31 figs. [63 refs.]

The main part of this work (nearly 70 pages) takes the form of a guide to the identification of the known species of *Anopheles* of French Guiana. It deals with some 20 species and contains descriptions of the morphological characters of the different stages, the breeding places, habits, relation to malaria transmission and their geographical distribution. There are also keys for the identification of the females, the males and the larvae.

In addition to the systematic part of the book there are notes on the history of *Anopheles* identification in South America, on elementary mosquito anatomy, on biology and on the techniques of collecting, rearing and preserving.

A note on the use of DDT states that *Aëdes aegypti* has disappeared from French Guiana and *Anopheles darlingi* is thought to have been eradicated from Cayenne.

H. S. Leeson

ROMEO VIAMONTE, J. M. & CASTRO, M. Estudio de la morfología de la armadura faríngea de algunos anofelinos. (Dipt. Culic.) [**Morphology of the Pharyngeal Armature of Certain Anophelines**] *Rev. Sanidad e Hig. Pública.* Madrid. 1951, June, v. 25, No. 6, 313-30, 12 figs. on 6 pls. [14 refs.]

The English summary appended to the paper is as follows :—

"In this paper the bucco-pharyngeal armatures of female Anophelines of several groups, some of which have not been studied anteriorly, such as



*Arthuromyia*, *Stethomyia*, *Myzorhynchella*, *Kerteszia* and *Chagasia* are described.

"The appropriate techniques of staining, dissection and mounting, to their best observation are explained.

"The different types of bucco-pharyngeal armatures observed are also presented, to, finally, revise the classification of them made by Sinton and Covell in 1928, amplifying to seven the five classes in which those authors divided them."

ROTH, L. M. & WILLIS, E. R. **Method for isolating Males and Females in Laboratory Colonies of *Aedes aegypti*.** *J. Econom. Entom.* 1952, Apr., v. 45, No. 2, 344-5, 1 fig.

It has been discovered that males of *Aedes aegypti* will respond to the sound of a tuning fork held near to the outside of the cage. They will then aggregate in a relatively small area on the cloth of the cage, from which they may be easily removed with an aspirator. By repeating the procedure of agitating the cage to induce flight, striking the tuning fork, and removing the males that are clinging to the side of the cage, a large number of males may be collected in a short time. Tuning forks between 320 and 512 vibrations per second are effective. With forks of a suitable frequency, this method might be extended to other species of mosquito.

A. J. P. Goodchild

TORRES CAÑAMARES, F. Le presencia del "*Aedes* (*Stegomyia*) *vittatus*" Big. en el Mediterráneo y algunas observaciones sobre el mismo. [**Observations on *Aedes vittatus* and its Presence in the Mediterranean**] *Rev. Sanidad e Hig. Pública.* Madrid. 1951, July-Aug., v. 25, Nos. 7/8, 435-43, 1 fig. [16 refs.]

PECKENSCHNEIDER, L. E., POKORNY, C. & HELLWIG, C. A. **Intestinal Infestation with Maggots of the "Cheese Fly" (*Piophilus casei*).** *J. Amer. Med. Ass.* 1952, May 17, v. 149, No. 3, 262-3, 3 figs.

DALMAT, H. T. **Notes on the Simuliidae (Diptera) of Guatemala, including Descriptions of Three New Species.** Reprinted from *Ann. Entom. Soc. of America.* 1951, Mar., v. 44, No. 1, 31-58, 23 figs. on 6 pls. [15 refs.]

PARROT, L. & BELLON, J. Notes sur les Phlébotomes. LXIV.—Phlébotomes du Ouaddaï. [**Notes on *Phlebotomus*. LXIV. *Phlebotomus* of Ouaddaï**] *Arch. Inst. Pasteur d'Algérie.* 1952, Mar., v. 30, No. 1, 60-63, 4 figs.

BRUCE-CHWATT, L. J. & ELLIOTT, R. **Insecticides in Public Health Practice in West Africa.** *Malaria Service Med. Dept. Nigeria. Information Bull.* No. 1. 1952, Feb., 26 mimeographed pp.

The regular use of insecticides against various disease vectors has become quite an important branch of public health, particularly in the tropics. The great advances in development of new insecticides in recent times have made the subject so extensive and complicated that most medical and sanitary officers greatly appreciate summaries and compilations of technical data.

The authors of this bulletin have produced a reasonably comprehensive and extremely practical guide to the choice of suitable insecticides and their efficient use for public health work. The introductory section deals with the general nature of the more important new synthetic insecticides. This is followed by details of the methods of formulation with simple rules for making up solutions, diluting concentrates and applying the correct doses in practice. For convenience, several tables of conversion factors and a glossary are added. There

follow some short paragraphs giving instructions for the use of insecticides against insect pests in West Africa, based on the authors' experience. Finally, an extensive table gives data about the composition, cost and price of a number of reputable commercial preparations.

J. R. Busvine

HOFFMAN, R. A. & LINDQUIST, A. W. **Absorption and Metabolism of DDT, Toxaphene, and Chlordane by Resistant House Flies as determined by Bioassay.** *J. Econom. Entom.* 1952, Apr., v. 45, No. 2, 233-5.

"The absorption and metabolism of DDT, toxaphene, and chlordane in resistant house flies, *Musca domestica* L., have been studied by a bioassay method using adult female house flies and *Aedes* mosquito larvae as test insects. Resistant flies topically treated with 10  $\mu$ gm of the toxicant were rinsed externally with acetone 4 or 24 hours after treatment, the flies were then macerated, and the absorbed toxicant extracted with acetone and removed by filtration. The mortalities obtained by topical treatment of susceptible flies with the extract were compared to a standard dosage-mortality curve obtained by treating susceptible flies with several known concentrations of insecticides. Resistant flies absorbed 5.4  $\mu$ gm of toxaphene, 3.8  $\mu$ gm of DDT, and 6.8  $\mu$ gm of chlordane. The bioassay method indicated that resistant flies metabolized 4.0  $\mu$ gm of toxaphene, 3.5  $\mu$ gm of DDT, and 5.9  $\mu$ gm of chlordane."

CARPENTER, S. J. & KEENAN, C. M. **Pre-Hatching Treatments with DDT Larvicides for the Control of *Aedes taeniorhynchus* (Wied.) in the Canal Zone.** *Mosquito News.* 1952, Mar., v. 12, No. 1, 15-16.

HOPKINS, L., NORTON, L. B. & GYRISCO, G. G. **Persistence of Insecticide Residues on Forage Crops.** *J. Econom. Entom.* 1952, Apr., v. 45, No. 2, 213-18, 1 fig.

LINDQUIST, A. W. **Radioactive Materials in Entomological Research.** *J. Econom. Entom.* 1952, Apr., v. 45, No. 2, 264-70. [25 refs.]

## LABORATORY PROCEDURES

LOEHNING, R. W. & VAN BAAREN, H. J. **A Simple Method for Staining Trypanosomes and Plasmodia of Malaria in Tissue Sections.** *Science.* 1952, Apr. 25, 469-70, 2 figs.

The authors claim that the following procedure will demonstrate trypanosomes and erythrocytic forms of malaria parasites in section of tissues better than any other methods :—

Small pieces of tissue are fixed in Helly's fluid for 10-12 hours and are then washed for 24 hours in running water. After dehydration in ethanol, the tissues are placed in varying concentrations of butyl alcohol in ethanol, then in pure butyl alcohol and are finally embedded in wax. (The use of butyl alcohol is said to prevent shrinkage of parasites.) The sections are stained with equal parts of Kingsley I and II [*Solution I* : Methylene blue 0.065 gm., methylene azure A 0.10 gm., glycerin 5 cc., methyl alcohol 5 cc., distilled water 25 cc. and buffer pH 6.9 15 cc. *Solution II* : Methylene violet (Bernthsen) 0.013 gm. eosin yellow W.S. 0.045 gm., glycerin 5 cc., methyl alcohol 10 cc., and acetone 35 cc. (*Stain Technology*, 1935, v. 10, 127)] for 5 minutes and are then quickly rinsed in 2 changes of distilled water (for malaria parasites they are differentiated for a few seconds in 1 per cent. acetic acid). The sections are quickly passed through acetone, acetone with eosin, butyl alcohol and 3 changes of neutralized xylol, and are then mounted.

P. C. C. Garnham

ALICNA, A. D. **Stain for Endamoebas.** *Med. Technicians Bull. Suppl. to U.S. Armed Forces Med. J.* 1952, May-June, v. 3, No. 3, 131-2, 1 fig.

The author stains intestinal protozoa with a modified Field's stain combined with an iodine preparation and since 1943 has found it "superior to any other stain, both in speed of application and in accuracy in the differentiation of the endamoebas". Trophozoites and cysts stain a yellowish green with dark brown to black nuclear material, chromatoid and glycogen bodies. Such preparations lend themselves well to photomicrography. The stain is prepared as follows :—

Solution 1 :	potassium iodide	...	...	...	...	8 gm.
	iodine	...	...	...	...	4 gm.
	distilled water	...	...	...	...	200 ml.
Solution 2 :	eosin	...	...	...	...	1 gm.
	anhydrous disodium phosphate	...	...	...	...	5 gm.
	anhydrous monobasic potassium phosphate	...	...	...	...	6.25 gm.
	distilled water	...	...	...	...	500 ml.

For use, 3 ml. of solution 2 are added to 9 ml. of solution 1. After thorough mixing the stain may be used immediately as a wet smear mixed with emulsified faeces or sigmoidoscopic material. The author has noticed occasionally that trophozoites of entamoebae have remained actively motile for a few moments even though the nuclear details were already stained. The differentiation of the elements in a cyst of *E. histolytica* is shown in a diagram. It is stated that the solutions will keep at 5°C. indefinitely, even after they have been mixed.

*H. J. O'D. Burke-Gaffney*

GRENIER, P. & TAUFFLIEB, R. Remarques sur les techniques modernes de montage rapide des insectes de l'utilisation des résines polyvinyliques en microscopie. [**Observations on Modern Techniques for Rapid Mounting of Insects and Use of Polyvinyl Resins in Microscopy**] *Bull. Soc. Path. Exot.* 1952, v. 45, No. 2, 208-12.

## REPORTS, SURVEYS AND MISCELLANEOUS PAPERS

STUDIES FROM INST. MED. RES. FEDERATION OF MALAYA. Jubilee Volume No. 25, pp. xiv+389, numerous figs. & 2 pls. 1951, Kuala Lumpur : Govt. Press. **The Institute for Medical Research 1900-1950 by various authors.** [Editorial Committee : FIELD, J. W., GREEN, R. & BYRON, F. E.]

The Director of the Institute, Dr. J. W. Field, and his colleagues, who have themselves made distinguished contributions to tropical medical research, have conceived the happy idea of publishing this volume in commemoration of the jubilee of the Institute, and in honour of their predecessors ; they have produced a most interesting and important book. We all know in general terms that the period 1900-1950 saw some of the greatest of developments in tropical medicine, and indeed in medicine generally, when the broad principles established in the 19th century were being applied and extended, but we tend to forget the details, and the steps of development are not always clear to a modern student. It is of the greatest value to read accounts such as are given



in this book of the course of modern medical history in Malaya, partly because that history is bound up with and therefore illuminates tropical medicine generally, and partly because it is an impressive justification of medical research. A sensitive reader could not finish the book without enhanced respect for the tropical research worker.

The volume is divided into sections. The first, by Field, gives the historical, racial and cultural background of Western medicine in Malaya; the second, also by Field, is a history of the Institute; the third (and by far the longest), by many authors, describes the historical trends of more than a score of diseases important in Malaya; the fourth, by Field, contains short biographies of the Directors of the Institute—Wright, Daniels, Fraser, Stanton, Fletcher, Kingsbury, Lewthwaite; and the fifth, also by Field, is an account of the Institute to-day. There are appendices on publications, the library, the staff from 1900 to 1950, and finance, and there is an index.

The standard of writing throughout is very high, and what might have become a somewhat arid catalogue of events and dates has been given a touch which has converted it into a fascinating story to be read with ease and pleasure. The events are striking enough, particularly, of course, the shrewd pioneering work of Watson in malaria; the astonishing piece of luck which brought the Kingsbury strain of *Proteus* quite by chance for use in the typhus fevers, and the outstanding chemotherapeutic work of Smadel, Lewthwaite and their team; and the hard thinking and clear experimentation of Braddon, Fraser and Stanton in beriberi. Besides these high-lights there are the numerous other researches and painstaking enquiries which have clarified and extended our knowledge of other diseases.

One of the pleasant features of the volume is the fact that the stories of work done by members of the staff of the Institute on the various subjects are incorporated with accounts of the trends of work on those subjects done elsewhere. The chapters in this volume, therefore, provide a conspectus of the general history of tropical medicine during the period, and if the emphasis is on the Malayan contribution, there is every justification for it. The record is indeed to be envied.

The whole is, of course, a history of the working of the expert and enquiring mind, and a most powerful though not explicitly stated argument for continuance and encouragement of research. It is also an acknowledgment of the importance of enlightened civil administration, such as was exercised by Swettenham with vision and power. It is sometimes fashionable to ignore the expert, and to argue that only the non-expert can see the wood for the trees, but the wide and scholarly approach of the authors of these chapters gives no support to that argument. Indeed, the experts have usually been ahead of their time, and one instance of this is indicated by the few sentences on p. 169 in which it is shown that the value of atebirin prophylaxis for military operations in highly malarious countries was appreciated in Malaya long before the war, but not by certain of the military authorities elsewhere until much later, when hard experience had taught a severe lesson.

The names of the authors of the various chapters are J. R. Audy, R. C. Burgess, F. E. Byron, J. A. Chelliah, J. W. Field, R. Green, J. L. Harrison, A. T. H. Marsden, D. S. Mankikar, J. A. Reid, S. R. Savoor, I. A. Simpson, R. H. Wharton, T. Wilson and Wu Lien-Teh. Special mention should be made of the numerous and excellent line drawings of people, buildings and landscapes by Yap Loy Fong, a member of the Staff of the Institute, and of the numerous photographs which illustrate the text. These distinguished contributors are sufficiently well known to guarantee the scientific standing of their contributions; they have clothed an impressive theme in language which matches its greatness.

Charles Wilcocks

CONGO BELGE. Fonds Reine Elisabeth pour l'Assistance Médicale aux Indigènes du Congo Belge. Rapport sur l'Activité durant l'année 1950 [DRICOT, C., Médecin-Directeur du Fonds en Afrique]. [**Report of the Activities of FOREAMI During 1950**] 124 pp., 16 pls., 2 maps (1 folding), 2 diagrams (1 folding) & 1 fig. [1952.] Brussels: 39, Rue du Commerce.

The past activities of FOREAMI have been previously reviewed [this *Bulletin*, 1951, v. 48, 595]. The stage of survey being complete, a 5-year plan of executive, curative and preventive work was started in 1948, and has progressed smoothly. The most interesting single event of 1950 was the establishment of a mobile radiography unit for the diagnosis of pulmonary tuberculosis in rural areas. The apparatus is mounted on two vehicles, is self-contained with generator, is completely air-conditioned, and can be used to take 1,000 miniature photographs a day, as well as normal radiographs. The results of some 25,000 examinations are classified by age, sex, and character of the lesion discovered, showing a total incidence of 0.5 per cent., a greater incidence among males than in females, and a progressively increasing incidence with age. Mantoux testing continued and classified findings are given, though the uniformity of reporting is criticized. BCG vaccination also continued but no opinion can yet be passed on its utility under bush conditions. The preliminary conclusions on tuberculosis are that the situation is not grave, the African reacts much as the European, and the work must continue.

The report describes the organization and its statistics, together with those of morbidity and mortality in the area served; the incidence of individual diseases as found by survey and hospital attendance; the activities of the associated industrial welfare organization; general welfare work; and demography, concluding with a statement of the original scientific work of the staff. There is much statistical detail on each subject together with constructive and often critical comment. It is notable that the endemic level of trypanosomiasis has reached a new low figure of 0.11 per cent., infection being confined to a few seed-beds, where energetic measures of chemoprophylaxis, treatment, and tsetse control are being taken. Malaria remains important, but chemoprophylaxis is preferred to mosquito destruction for its control, the most generally used drug being Nivaquine [chloroquine sulphate] which is commonly given in solution. Yaws is being largely treated with single doses of 2.4 million units of slow penicillin, and leprosy with diamino-diphenylsulphone, the results of both treatments promising well for ultimate control of the diseases.

ANDRÉ gives an account of Mantoux testing and BCG vaccination, together with a statement of the effect on the tuberculin reaction of vaccination by intradermal inoculation and by scarification. The former proved more effective and the method is approved for use in the Congo.

HIMPE, WEBER and CAHAY give an account of the use of DDT smoke bombs against tsetse flies. They contained 450 grammes of a combustible powder of which 50 per cent. was DDT, and were ignited in the neighbourhood of water points frequented by flies. Results were measured by counts of flies before and after fumigation, and though some trials were very promising the results were highly irregular, and insufficiently reliable to justify continuation.

G. Macdonald

EAST AFRICA HIGH COMMISSION. **East African Malaria Unit Annual Report 1951** [WILSON, D. Bagster, Director]. 9 pp., 1 fig. 1952. Nairobi: Govt. Printer.

The new East African Malaria Unit came into full operation in 1951. It has accommodation at Amani and Muheza in the Tanga Province of Tanganyika, some details of each place being given, and has the functions of training,

research, and provision of specialist advice to the Governments of Tanganyika, Kenya and Uganda. Training is primarily intended for African staff likely to be engaged in malaria control, and classes began in the year reviewed.

The staff consists of a Director, an Entomologist, two Field Officers and one Engineer. Research on anopheline bionomics is reviewed below; other work included the establishment of a laboratory colony of *Anopheles gambiae*, malaria surveys in the territories concerned and in British Somaliland, an experiment in the use of BHC against *A. gambiae*, and an experiment in control of breeding of that anopheline by DDT applied from aircraft, which had inconclusive results.

GILLIES reports on studies of *A. gambiae* and *A. funestus*. Estimations of the use of outside resting places by means of traps suggest that free use is made of them by unfed and gravid females, but that feeding is primarily on occupants of houses and the mosquitoes rarely leave the house until some considerable time after feeding. The normal gonotrophic cycle lasts 3 days when the mean monthly temperature is below 74°F. (*A. gambiae*) or 77°F. (*A. funestus*), and 2 days when these temperatures are exceeded. A single blood meal is taken in each cycle, but it may be that newly emerged females need more than one meal to enable them to complete the first ovarian development. A number of adults are found in all surveys, which are fertilized and fed, but have not passed Stage II of ovarian development. They are thought to have taken one meal only and are described as *pregravid*. Further work on these lines, and on anopheline longevity, is in progress.

[The new Unit marks its first year of full operation by an interesting and valuable report, which augurs well for the success which the Editor and reviewer wish it.]

G. Macdonald

NEW YORK STATE DEPT. OF HEALTH. **Laboratory Manual for Physicians. Aids in Diagnosis and Treatment.** Tenth Edition. pp. v+80, 1 fig. 1951. Issued by Division of Laboratories and Research, Albany. [This review appears also in *Bulletin of Hygiene*.]

This extremely informative manual differs in many details from its predecessor [this *Bulletin*, 1949, v. 46, 192], especially in the additional attention given to virus diseases. It is noted that "the radical changes in microbiology, the development of biochemical concepts of immunity, bacteria nutrition and growth, and the significant new knowledge of bacterial antagonism and host-parasite relationships have but little affected the basic examinations used as aids in diagnosis". The authors, very properly, while adding new knowledge have retained most of the old, so that the manual still remains a full compendium of information on the services provided and the means of and indications for obtaining them. The sections of the manual follow similar, but broader, lines than those of the 9th Edition, and the inclusion of new knowledge is noteworthy.

There are now 150 local medical laboratories provided by New York State and there were no less than 8 million tests performed in 1950.

The importance of close linkage between laboratory, public health service and clinical medicine is stressed once more and it is rightly pointed out that laboratory diagnosis of disease is "the hard core of much medical and surgical practice".

H. J. O'D. Burke-Gaffney

KARK, S. L. & CASSEL, J. **The Pholela Health Centre. A Progress Report.** *South African Med. J.* 1952, Feb. 9 & 16, v. 26, Nos. 6 & 7, 101-4; 131-6.

The Pholela Health Centre in Natal, South Africa, is now well known, and has, in fact, been regarded as the model for the centres which have been pro-



posed for other parts of the Union [see this *Bulletin*, 1944, v. 41, 611 ; 1946, v. 43, 162]. The Centre provides a general service of out-patient treatment of the sick, with special sessions for maternity and infant welfare work, and a family health and medical care programme for the 8,500 people of the district. Home visits are a particular feature of the service, and stress is laid on education. The work entails control of communicable diseases, including syphilis and tuberculosis, and a nutrition programme. Doctors, nurses and health assistants are employed ; they have come to know intimately the people with whom they deal, and they have observed them over a period of 11 years.

In this period the infant mortality rate has fallen from 27.5 to 10.06 per 100 live births [the rate is expressed thus, rather than in the conventional way per 1,000 live births]. The crude general death rate has also fallen, but the trend is complicated by a bad year at the beginning of the period of observation, and by the constant influx of new families, which tends to mask the figures for the families longer under observation, which show the best trend. During this period there has been a marked reduction in the number of patients treated for malnutrition, and although the food position is by no means good, much has been done to introduce new and better foods and to break down old tribal taboos which were unfavourable to good nutrition.

The authors name two most significant factors in relation to the health of these Africans, namely soil erosion and the system of migrant labour under which many men leave their families to work in towns, and bring back the diseases of the towns, especially venereal diseases and tuberculosis. These factors have led to malnutrition and to maladjustment in family relationships in addition to the communicable diseases ; their removal or amelioration is a national problem, and medical and educational effort such as is expended so usefully by the staff of this Centre can hope only to mitigate their effects.

This work surely deserves every encouragement.

*Charles Wilcocks*

ADAMS, P. C. G. **Disease Concepts among Africans in the Protectorate of Northern Rhodesia.** *Rhodes-Livingstone J.* 1950, No. 10, 14-50, 1 folding map.

One of the most important of the activities of the medical and public health services in Africa is the education of the people in Western conceptions of the causation of disease, and the means to be taken for prevention. This education is partly achieved, of course, by instruction of special groups of people, including hospital attendants and sanitary inspectors, and partly by the teaching of children in schools. It is, perhaps, too often assumed that the instruction given is received and assimilated without special difficulty, but the author of the present paper produces evidence which suggests that the conceptions which Western minds now accept are introduced to Africans who have already been very strongly taught quite other beliefs, and that before the new ideas can hope to carry conviction they must supplant these strongly held opinions. The intellectual difficulty of this process is heightened by the fact that the traditional African conceptions of disease are closely associated with witchcraft, taboo and belief in spirits, that these factors hold a strong element of fear, and that the beliefs are instilled in childhood when impressions are powerfully incorporated into the psychological framework.

The author, who is Superintendent Tutor at the African Medical Training School in Lusaka, N. Rhodesia, made enquiries into the opinions held by 29 senior and 14 junior students as to the causation of diseases. These students had received many years' education (average  $10\frac{1}{2}$  for the seniors) on Western lines, but most of them admitted the opinion that the chief causes of disease

were witchcraft, spirits and broken taboo. A number of them wrote essays on the beliefs of their own tribes in this respect, and parts of these are reproduced. They show how strong is the mental conditioning to which children are subjected, and how great is the difficulty which must be experienced by those students who do eventually throw over their traditional beliefs and accept the new instruction. [The reviewer wonders if, indeed, this change can truly be effected in the present generation; it has taken longer in Europe. In the meantime it is essential to continue to instruct the Africans in the hope that future generations will benefit, but for the present instruction must be accompanied by careful supervision.]

The author is not discussing the education of African medical men, who perhaps more than anybody else may influence their people. He has made a new and important factual contribution to this difficult subject.

Charles Wilcocks

ANALYSIS OF THE DISEASE CONCEPTS AMONG AFRICANS IN THE PROTESTANT COLLEGE, NAIROBI, KENYA, 1950-1951

One of the most important of the problems of the medical and public health services in Africa is the education of the people in the concepts of disease and its causation. It is essential to be clear for the purpose of this education. The education is partly achieved by instruction of groups of people, including medical students and health workers, and partly by the teaching of individuals. It is not possible to assume that the education given is readily and immediately accepted, but the author of the present paper provides evidence to suggest that the concepts which Western medical men introduce to Africans who have already been very strongly taught quite other beliefs, and that before the new ideas can hope to carry conviction they must supplant those already held. The historical continuity of the process is highlighted by the fact that the traditional African concepts of disease are closely associated with witchcraft, taboo and belief in spirits, that these factors hold a strong position in the beliefs of the people in childhood when impressions are being fully imprinted into the psychological framework.

The author, who is Superintendent Tutor at the African Medical Training School in Nairobi, N. Rhodesia, makes reference to the opinions of other workers and to further students in the literature of the subject. The work is well written and is a valuable contribution to the subject.

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# ALPHABETICAL LIST OF AUTHORS OR SOURCES

- Adams, A. R. D., (866).  
 Adams, P. C. G., 915.  
 Agosin, M., Christen, R., Jarpa, A., Atias, V. A. & Neghme, A., 849.  
 Ajello, L., 895.  
 Alicia, A. D., 911.  
 Amies, C., Murray, N. L., Scott, J. G. & Warren, R. St. H., 897.  
 de Andrade, L., 897.  
 Anneck, S. & Quin, P., 869.  
 Ansari, N. & Faguib, 849.  
 Antonini, F., (862).  
 Baloch, G. M. K., 894.  
 Barton, W. L., 878.  
 Baussay, J., 853.  
 Beaver, P. C., 885.  
 — & Sodeman, W. A., 884.  
 Berberian, D. A., Dennis, E. W., Korn, R. F. & Angelo, C. A., 867.  
 Bertrand, M., 902.  
 Blanc, F. & Martin, M., 863.  
 Blumberg, B., McGiff, J. & Guicherit, I., 838.  
 Boenjamin, R., (872).  
 Bruce-Chwatt, L. J. & Elliott, R., 909.  
 Budden, F. H., 896.  
 Caminopetros, J., 893.  
 Carpenter, S. J. & Keenan, C. M., (910).  
 Castellani, A., (902).  
 Chang, H. F., 883.  
 Ch'in, K. Y., Liu, W. & Liu, Y., 853.  
 Chung, H. & Feng, L., with Feng, S., 840.  
 Clavié, L. C., 903.  
 Congo Belge, 913.  
 Crosnier, R., Darbon, A., Ducournau, P. & Costerousse, L., 863.  
 Crozes & Guth, 904.  
 Dalmat, H. T., (909).  
 Darzins, E. & Bismans, J., 856.  
 Das, A. & Roy, S. K., 856.  
 Deane, L. M., 887.  
 Dejou, L., (888).  
 Dobell, C. (The Late), 859.  
 Dricot, C., 913.  
 Duke-Elder, S., Ainslie, D. & Boase, A. J., 900.  
 East Africa High Commission, 913.  
 Elton, N. W., 856.  
 Faust, E. C., 861.  
 Fellers, F. X., 853.  
 Field, J. W., Green, R. & Byron, F. E., 911.  
 Findlay, G. M. & Howard, E. M., 855.  
 Floch, H., 875.  
 — & Abonnenc, E., 908.  
 — & Destombes, P., 872.  
 — & Horth, R., 874.  
 — & Lecuiller, A., 874.  
 Foy, H. & Kondi, A., 842.  
 — & Hargreaves, A., 892.  
 Fuchs, A., 896.  
 Gerber, J. H., 875.  
 Gilroy, A. B., 844.  
 Giroud, P. & Gaillard, J. A., 907.  
 Gohar, M. A., Eissa, A. A. & Sebai, I., 878.  
 Greiner, H., 884.  
 Grenier, P. & Taufflieb, R., (911).  
 Hall, W. H. & Loomis, G. W., 838.  
 Hansen, E. L. & Bennett, B. M., 866.  
 Hanson, R. O. & Tatum, A. L., 846.  
 Harris, B. P., (858).  
 Harris, F. C., 878.  
 Harris, R. S., 891.  
 Hawking, F., 890.  
 Heim de Balsac, H., Le Gac, P. & Giroud, P., (857).  
 Hein, W., 906.  
 Helluy, J. R. & Schwartz, J., 858.  
 Henrard, C., 847.  
 Henry, A. J., Mansour, R., Watson, A. G. & Zaki, A. H., 851.  
 Hens Tienda, L. & Fernández Nafria, A., 871.  
 Hoffman, R. A. & Lindquist, A. W., 910.  
 Holz, J., 904.  
 Hood, M., (883).  
 Hopkins, L., Norton, L. B. & Gyrisco, G. G., (910).  
 Hoü, H. F., Li, S. Y., Wang, C. K., Fan, P. C. & Huang, T. C., 878.  
 Huard, P., Vu-Cong-Hoe & Tran-Anh, 838.  
 Humphry, A. H., 871.  
 Hunter, G. W., Kaufman, E. H., Jr. & Pan, C., 879.  
 James, T., 891.  
 Jeffery, G. M., 840.  
 Jelliffe, D. B., 855.  
 Jones, W. R., 866.  
 Jussiant & Gaspard, (848).  
 Kagioka, T., Miki, T. & Yoshida, S., 885.  
 Kalra, S. L. & Jacob, V. P., 869.  
 — & Rao, K. N. A., 868.  
 Kark, S. L. & Cassel, J., 914.  
 Kerr, K. B. & Cavett, J. W., 886.  
 Kershaw, W. E., 888.  
 Knutson, H. & Szymkowitz, R. T., 857.  
 Koerber, R., 902.  
 Kraneveld, F. C., Houwink, A. L. & Keidel, H. J. W., 848.  
 Krüpe, M., 840.  
 Kumm, H. W., 855.  
 Lachmajerowa, J. [Lachmajer, J.], 838.  
 Lelong, M. & Desmonts, G., 905.  
 Levaditi, C., Vaisman, A. & Henry-Eveno, J., (856) *bis*.  
 Lindquist, A. W., (910).  
 Lipparoni, E., 843.  
 Loehning, R. W. & van Baaren, H. J., 910.  
 Lowe, J., (871).  
 Lubinski, G., 859.  
 Lüdicke, M. & Piekarski, G., 839.  
 Lund, E., 862.  
 Macdonald, G., 813.  
 McFadzean, J. A., 886.  
 Mackie, A. & Raeburn, J., 882 *bis*.  
 McVay, L. V., Jr. & Sprunt, D. H., 867.  
 Maegraith, B., 847.  
 Malard, A., 852.  
 Malfatti, M. G., (872).  
 Mara, M., 837.  
 Mehlman, B. & von Brand, T., (876).  
 Meloney, H. E., Moore, D. V., Moat, H. & Carney, B. H., 880.  
 Mendoza, J. B., 843.  
 Mercado, T. I. & Coatney, G. R., 844.  
 Miyazaki, I., 884.  
 Mohr, W., 842.  
 Moise, R., 837.  
 Møller-Christensen, V. & Faber, B., 872.  
 Montestruc, E. & Saint-Cyr, C., 903.  
 Moore, D. V. & Meloney, H. E., 877.  
 Murgatroyd, F., (842).  
 Nasir-Ud-Din, M., 843.  
 Nauck, E. G., (854).  
 Neal, R. A., 860.  
 — & Hoare, C. A., 859.  
 Neghme, A., Agosin, M., Christen, R. & Rubio, M., 868.  
 New York State Dept. of Health, 914.  
 Oddo, F. G. & Bruno-Smiraglia, C., 845.  
 Parrot, L. & Bellon, J., (909).  
 Patel, J. C., (888).  
 Peckenschneider, L. E., Pokorny, C. & Hellwig, C. A., (909).  
 Perepérez Palau, F., 853.  
 Pesce, H., 872.  
 Pessoa, S. B. & Coutinho, J. O., 876.  
 Peters, D. & Wigand, R., 854.  
 Pollitzer, R., 857.  
 Portugal, H., 873.  
 Pupo, J. de A., 874.



# ALPHABETICAL LIST OF AUTHORS OR SOURCES—*cont. from page 3*

- Raffaele, G., 840.  
 Rao, K. N. A., (853).  
 Raper, A. B., (893).  
 Reardon, L. V., Verder, E. & Rees, C. W., 860.  
 Reiss, H. J. & Verron, G., 906.  
 Rev. Brasileira Leprologia, 870.  
 Rhodes, K., 892.  
 Ritchie, L. S., Hunter, G. W., Kaufman, E. H., Jr., Fan, C., Nagano, K., Yokogawa, M. & Szwczak, J. T., with Hishinuma, Y., Shimizu, M. & Asakura, S., 881.  
 Romeo Viamonte, J. M. & Castro, M., 908.  
 Roovers, J. J. C. P. A. & van Steenis, P. B., 863.  
 Roth, L. M. & Willis, E. R., 909.  
 Rozeboom, L. E., 839.  
 Rudra, M. N., Chowdhury, L. M. & Sinha, S. P., 904.  
 Saiz Moreno, L., (884).  
 Sampaio, S., de Souza Lima, L. & Nahas, L., 873.  
 Sarkies, J. W. R., 896, 901.  
 Schorr, S. & Schwartz, A., 861.  
 Shah, M. A., 901.  
 Shibata, S., 841.  
 Siggia, S. & Mamola, P., (901).  
 Signier, F., Feld, Piette, M., Welti, J. J. & Lumbroso, P., 882.  
 Simonet, P., 852.  
 Soong, H. Y. & Ho, E. A., 851.  
 Soper, F. L., 855.  
 Sorsby, A., 898.  
 Souza Campos, N., 873.  
 Stone, H. H., Tool, C. D. & Pugsley, W. S., 851.  
 Straub, W., 906.  
 Studies from Inst. Med. Res. Federation of Malaya, 911.  
 Tanaka, H., Ikuzawa, M. & Moriya, S., (857).  
 ——— & Sumiyoshi, K., (857).  
 Teesdale, C., 869.  
 Terzian, L. A., Stahler, N. & Ward, P. A., 846.  
 Thompson, M. D. & Trowell, H. C., 891.  
 Tobie, E. J., 848.  
 Torres Cañamares, F., (909).  
 Torres Estrada, A., 841.  
 Tosteson, D. C., Shea, E. & Darling, R. C., (893).  
 Trope, R. A., 900 *bis*.  
 Vaněk, J. & Jirovec, O., 908.  
 Vu-Cong-Hoe, 887.  
 Wenger, H., 864.  
 Westphal, A. & Bauer, F., 905.  
 Wilson, D. B., 913.  
 Woodruff, A. W., (890).  
 Woodward, S. F., 894.  
 Zavala, D. C. & Hamilton, H. E., 862.

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